# EVALUATION OF BODE INDEX AS A PREDICTOR OF SEVERITY AND ITS CORRELATION WITH PULMONARY HYPERTENSION IN COPD PATIENTS

**A Dissertation Submitted to**

**THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY**

**CHENNAI**

*In Partial Fulfillment of the Regulations*

*For the Award of the Degree of*

**M.D. (GENERAL MEDICINE) - BRANCH – I**

**GOVERNMENT KILPAUK MEDICAL COLLEGE**

**CHENNAI**

**MAY 2019**

# BONAFIDE CERTIFICATE

This is to certify that "**EVALUATION OF BODE INDEX AS A PREDICTOR OF SEVERITY AND ITS CORRELATION WITH PULMONARY HYPERTENSION IN COPD PATIENTS"** is a bonafide work done by **Dr. K. PALANI** Post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in partial fulfillment of rules and regulations of the TamilNadu Dr. M.G.R Medical University, for the award of M.D. Degree Branch I (General Medicine) during the academic period from MAY 2016 To MAY 2019.

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# DECLARATION

I solemnly declare that this dissertation **"EVALUATION OF BODE INDEX AS A PREDICTOR OF SEVERITY AND ITS CORRELATION WITH PULMONARY HYPERTENSION IN COPD PATIENTS"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof. Dr. T.S. SANTHI, M.D,** Professor of General Medicine, Department of Internal Medicine, Government Kilpauk Medical College and Hospital, Chennai. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

Place: Chennai-10 **Dr. K. PALANI**

Date :

# CERTIFICATE BY THE GUIDE

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An open labelled,randomised,prospective study comparing the efficacy and safety of doxofylline with theophylline in COPD patients.pdf (D31351600)
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**Protocol ID. No. 06/2018 Meeting held on 08.01.2018**

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "EVALUATION OF BODE INDEX AS A PREDICTOR OF SEVERITY AND ITS CORRELATION WITH PULMONARY HYPERTENSION IN COPD PATIENTS" submitted by Dr.K.PALANI, Post Graduate in General Medicine. Govt. Kilpauk Medical College, Chennai-10.

The Proposal is **APPROVED.**

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

**DEAN**
**Govt. Kilpauk Medical College,**
**Chennai-10.**

ME 1 Sec> Ethical Committee

# ABBREVATIONS

| | | |
|---|---|---|
| COPD | – | CHRONIC OBSTRUCTIVE PULMONARY DISEASE |
| BMI | – | BODY MASS INDEX |
| FEV1 | – | FORCED EXPIRATORY VOLUME IN 1 SECOND |
| FVC | – | FORCED VITAL CAPACITY |
| PHT | – | PULMONARY HYPERTENSION |
| TLC | – | TOTAL LUNG CAPACITY |
| RAD | – | RIGHT AXIS DEVIATION |
| CTPA | – | COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAM |
| GOLD | – | GLOBAL INITIATIVE FOR LUNG DISEASES |
| WHO | – | WORLD HEALTH ORGANISATION |

# ACKNOWLEDGEMENT

At the outset, I would like to thank my beloved Dean, Kilpauk Medical College & Hospital, **PROF.DR.P.VASANTHAMANI, M. D., D.G.O., MNAMS.,DCPSY.,MBA** for her kind permission to conduct the study in Kilpauk Medical College.

I express my indebtedness to **Prof. Dr. K.V. RAJALAKSHMI M.D,** Professor & HOD of Medicine, Department of General Medicine, Kilpauk Medical College & Hospital for permitting me to carry out this study and for her constant encouragement and guidance.

I owe my sincere thanks and gratitude to my Guide, **Prof. Dr. T.S. SANTHI M.D,** Professor of Medicine, Kilpauk Medical College & Hospital for her continuous motivation, affectionate guidance, valuable suggestions, sympathetic, helping nature and encouragement enabled me to complete the dissertation.

I sincerely thank **Prof. Dr. V. MEERA M.D., D.G.O.,** Professor and Head, Department of Biochemistry, Kilpauk Medical College, for providing valuable time, knowledge & assistance without which it would not have been possible to have this study started. Also a special thanks to her for her love, care and affection on me.

I also express my sincere gratitude to **Prof. Dr. K.E. Govindarajulu M.D., Prof. Dr. S. Chandrasekar M.D.,** for their help and guidance rendered during the entire period of my work.

I sincerely thank **Prof. Dr. T. Ravindran M.D., DNB** for his constant support in all the stages.

I am extremely thankful to my Assistant Professors, **Dr. M. Bathragiri M .D., Dr. G. Gurunamasivayam MD., DPM., Dr. R. Poongundran M.D., Dr. R. Vijayakumar M.D., Dr. T. Mohanasundaram M.D., D.A., Dr. P. Boopathi Rajan M.D., DTCD** for their valuable suggestions and guidance in completing this thesis work.

A very special thanks to my Father, Mother, Brother and Sister in law for their valuable support.

A special thanks for **Dr. E. Arumugam, Dr. Ellan Shiv Goutham & Dr. Tamilmathy Goutham** for their everlasting support & love on me.

I also extend my sincere thanks to **Dr. P. Rajkumar & Dr. S. Krishna Kumar** who helped me in completing this thesis.

I sincerely thank my Co-PGs **Dr. A.S. Nath, Dr. P. Pavithra, Dr. R. Narayanee, Dr. G. Arun, Dr. P. Kalpana, Dr. S. Balamurugan**

**& Dr. R. Prabakaran,** my Seniors **Dr. S. Charan Kumar, Dr. R. Priyadharshini, Dr. R. Sharmila Devi, Dr. Sowmya Sridharan & Dr. J. Arun Kumar** and my Juniors **Dr. A. Ashwini, Dr. A. Abhishek, Dr. S.Veeraselvan, Dr. R.G. Rajasekar & Dr. P. Rashika** for their valuable support during my entire PG period.

I would always remember with extreme sense of thankfulness for the valuable time, co-operation, criticism and support provided by my fellow post graduates, juniors, C.R.R.I's and friends.

I also extend my thanks to all the laboratory technicians for their valuable support throughout my dissertation work.

I would like to take this opportunity to show gratitude to my friends & family for their never ending support in completing this thesis.

Finally, I wholeheartedly thank all my patients for their active cooperation in this study, without whom this would not have become a reality.

# TABLE OF CONTENTS

# INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of mortality and morbidity and health care costs worldwide. The prevalence of COPD are projected to increase in the coming years due to continued exposure to pollutants and the changing age and lifestyle structure of the population. As the population bulges the disease progression rate is also increasing. It is projected to rank third in 2020, according to a study published by the World Bank/World Health Organisation (WHO).1 COPD causes a heavy burden on the global health care resources. The costs involved in the evaluation as well as treatment is directly proportional to the various components of the disease.2

'Chronic obstructive pulmonary disease (COPD) is defined as a treatable and preventable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients'. The pulmonary component is characterized by airflow limitation which is not fully reversible. There is progressive airflow limitation that is usually associated with an abnormal inflammatory response of the lung to noxious agents or gases.3 COPD is not simply a "Smoker's cough" but a life threatening illness that exhibits a wide range of Iceberg phenomenon. As in other chronic inflammatory conditions, weight loss, muscle wasting, hypoproteinemia and tissue depletion are commonly seen in COPD patients.

The COPD severity is generally assessed on the basis of a single parameter i.e forced expiratory volume in one second (FEV1). However, the systemic

manifestations of COPD were not reflected by the FEV1. Hence, a multidimensional grading system which assesses the respiratory and systemic expressions of COPD is designed to predict outcome in these patients.4 The four factors that predicted the severity most were the Body-mass index (B), the degree of airflow obstruction (O) and dyspnea (D) and exercise capacity (E), measured by the six-minute–walk test. These variables were used to construct the multidimensional BODE index which is a 10-point scale in which higher scores indicate the more severe nature of the disease and higher risk of death.

The process of allocating scarce medical resources to the most needed patients can be extremely difficult in diseases which affect a large number of patients. Decision makers need a rational and consistent scoring system that is designed to identify those who are maximally in need of a therapeutic or a diagnostic intervention under a health-care budget constraint in a developing country like India. BODE index has been proposed to serve this purpose in patients with Chronic Obstructive Pulmonary Disease (COPD).5 BODE Index assessment is a bedisde test that can be applied in all patients with COPD at any primary care level where Echocardiogram is not possible, hence grading the patient severity by BODE Index will be very much useful in early diagnosis and prevention of its systemic complications.

In this study, the severity of COPD and its systemic effects (PHT) were considered and its correlation with BODE Index as a predictor were carried out.

# AIMS AND OBJECTIVES

- To compare the severity of COPD using BODE index than primary lung function test alone.
- To determine whether higher BODE index in chronic obstructive pulmonary disease correlates with more years of cigarette smoking and more days of hospitalisation.
- To determine whether higher BODE index is associated with more severe systemic compilcations in the form of cardiac involvement (PHT).

# REVIEW OF LITERATURE

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic obstruction of airflow that interferes with normal breathing which is not fully reversible. COPD is one of the leading causes of mortality and morbidity worldwide and imparts a substantial economic burden on society and individuals.

## DEFINITION

Chronic obstructive pulmonary disease (COPD) was initially defined as "a disease state characterized by chronic airflow limitation due to chronic bronchitis and emphysema". Chronic bronchitis has been defined in clinical terms as 'the presence of chronic productive cough for atleast 3 consecutive months in 2 consecutive years. Other causes of chronic productive cough must be ruled out'. Emphysema, on the other hand, has been defined by its pathologic description: 'an abnormal enlargement of the air spaces distal to the terminal bronchioles accompanied by destruction of their walls and without obvious fibrosis'.

However, the definition of COPD has undergone major revision. The new GOLD guidelines[3] and the ATS/ERS definition[5] reflect these scientific advances: "Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by

airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases".[3] While the new guidelines do not specifically include chronic bronchitis and emphysema in the definition of COPD, it is made clear that they are considered the predominant causes of COPD.

The airflow limitation is caused by mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema) the relative contribution of each varies from person to person.[3]

**EPIDEMIOLOGY**

Using the World Health Organization/World Bank Global Burden of Disease Study data, the worldwide prevalence of COPD in 1990 was estimated at 9.34/1000 in men and 7.33/1000 in women.[6,7] This was an underestimation of true prevalence of COPD since the estimates included all age groups.

In a large epidemiologic study from Korea involving 9,243 subjects, Kim and his colleagues reported that the prevalence of COPD was 17.2% among subjects older than 45 years.[8] There is plenty of information on the prevalence and burden of COPD from the developed countries. Such an assessment is rather scarce from most of the developing world.

The prevalence of COPD reported in different population based studies from India is highly variable.[9] The prevalence rates in male subjects of 2.12% to

9.4% in studies reported from the North are generally higher than 1.4% to 4.08% reported from South India. The respective ranges for female subjects vary from 1.33% to 4.9% in the North and from 2.55% to 2.7% in South India. For epidemiological assessment, the rounded-off median prevalence rates were assessed as 5 percent for male and 2.7 percent for female subjects of over 30 years of age.[9] The disease is distinctly more common in males.

The prevalence was found to increase with increasing age, especially the males, in those with more than 20 pack–yrs of smoking and in low income subjects. The male to female ratio had varied from 1.32:1 to 2.6:1 in different studies with a median ratio of 1.6:1.[9]

**RISK FACTORS**

A. **Genetic risk factor**: A rare recessive, severe deficiency of alpha-1 antitrypsin[9], which is a major circulating inhibitor of serine proteases, most commonly seen in individuals of Northern European origin.[10]

B. **Exposure to environmental particles**

**Tobacco smoke**: Cigarette smokers have a greater annual rate of decline in $FEV_1$ and a greater COPD mortality rate than non-smokers.[11,12] Not all smokers develop clinically significant COPD, which suggests that genetic factors must modify each individual's risk.[13] Passive exposure to cigarette smoke may also contribute to

respiratory symptoms[14] and COPD[15] by increasing the lungs' total burden of inhaled particles and gases.[16,17]

**Occupational dusts organic and inorganic chemicals**: A statement published by the American Thoracic Society concluded that occupational exposures account for 10-20% of either symptoms or functional impairment consistent with COPD.[18]

**Indoor and Outdoor Air Pollution**: The evidence that indoor pollution from biomass cooking and heating in poorly ventilated dwellings and high levels of urban pollution is an important risk factor for COPD.[19-25] This has been proved by many case-control studies[24,25] and other robustly designed studies.

C. **Gender**: Studies from developed countries[26] show that the prevalence of the disease is now almost equal in men and women. Some studies have suggested that women are more susceptible to the effects of tobacco smoke than men.[27-29]

D. **Infection**: A history of severe childhood respiratory infection has been associated with COPD.[30-32]

E. **Low birth weight**

F. **Socioeconomic Status**: The risk of developing COPD is inversely related to socio-economic status.[33-35]

G. **Poor nutritional status**

H. **Comorbidities**

**SYMPTOMS**

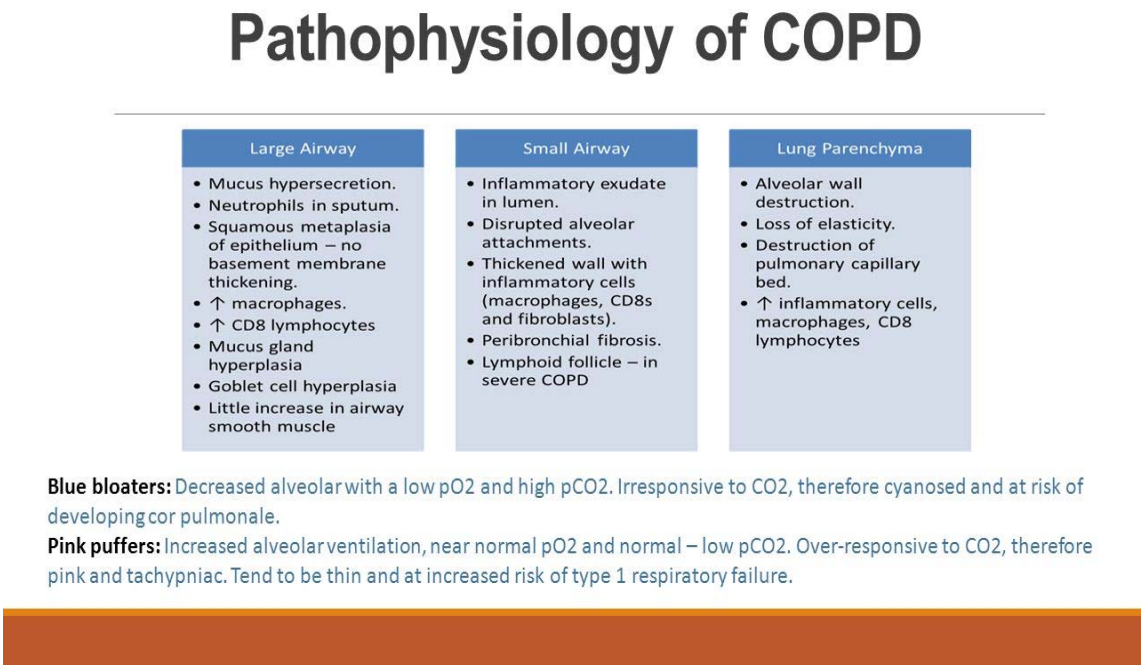
Key symptoms include: Patient is usually a long-time heavy smoker who presents with anyone of the following:

- Long-term (chronic) cough.
- Chronic mucus (sputum) production.
- Morning "smoker's cough".
- At least one episode of "bronchitis" every winter.
- Repeated episodes of acute bronchitis.
- Wheezing and Shortness of breath that is persistent and gets worse, occurs during exercise, and gets worse during respiratory infections.
- Shallow cough with the feeling that something is stuck inside the chest.

Patients may have a rapid, sometimes sudden, and prolonged increase in symptoms (cough, amount of mucus, and/or shortness of breath), especially if the COPD is mainly chronic bronchitis. This is called a COPD exacerbation.

## PATHOPHYSIOLOGY OF COPD

Quantitative evidence of increased expiratory flow resistance in emphysema was first obtained in one patient by Neergard and Wirz in 1927.[36] In 1934, Christie described elastic properties or distensibility of the lung in emphysema.[37] The "golden age" of pulmonary macrophysiology, extending from about the 1960s to the 1980s provided new insights regarding the determinants of flow limitation at the levels of the airway and parenchyma. Corbin and co-workers showed that smoking was associated with the loss of lung recoil pressure and with increased static lung volumes (RV, FRC, and TLC), even among individuals who had relatively normal $FEV_1$.[38] Upto a point, these changes appeared reversible with smoking cessation.



COPD, or chronic obstructive pulmonary disease, is a progressive inflammatory disease connecting the airways, lung parenchyma, and vasculature. It causes the damage and remodelling of the airways and lung tissue. The inflammatory process is a driving aspect in the pathophysiology of COPD. Recent verification suggests that the inflammatory response results in a number of effects, including an arrival of inflammatory cells such as macrophages, neutrophils and lymphocytes. Thickened airways and structural changes such as increased smooth muscle and fibrosis may also be manifested.

Cigarette smoking causes an inflammatory response in the lungs. This response does not cease with the removal of the stimulus, but progresses for an unlimited period of time. These processes result in emphysema, chronic bronchitis, or both. Emphysema begins with a small airway disease and progresses to alveolar destruction, with a predominance of small airway narrowing and mucous gland hyperplasia.

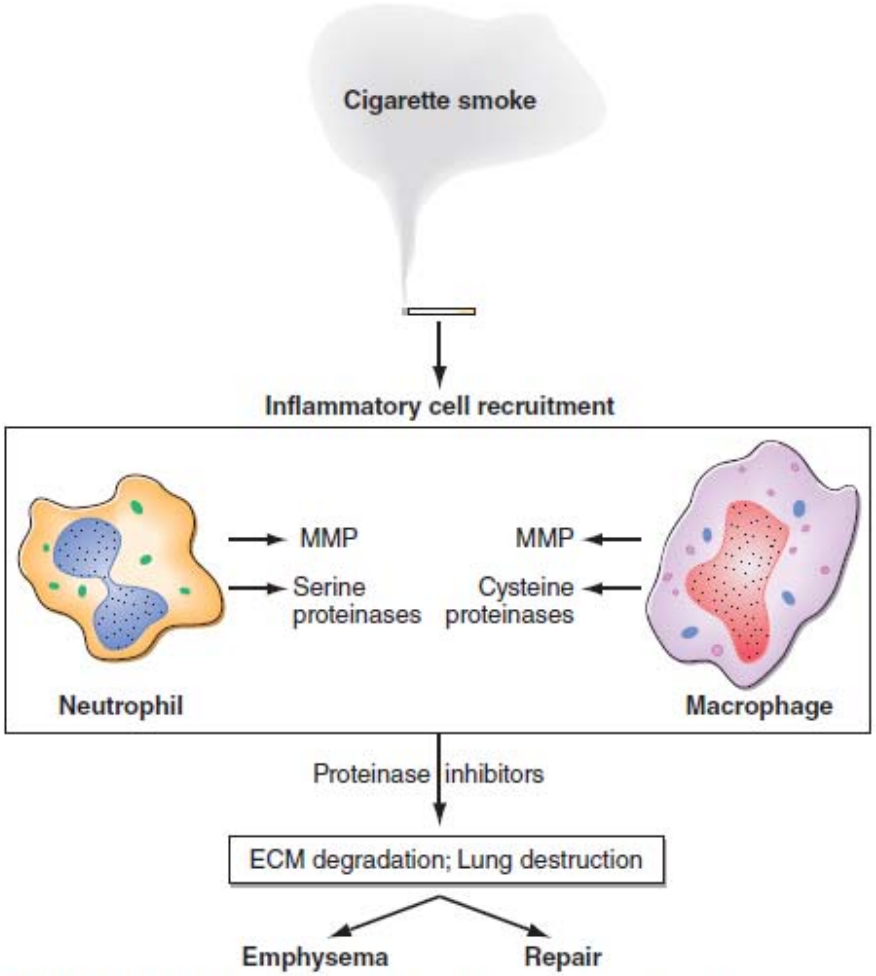



**FIGURE 314-1 Pathogenesis of emphysema.** Upon long-term exposure to cigarette smoke, inflammatory cells are recruited to the lung; they release proteinases in excess of inhibitors, and if repair is abnormal, this leads to air space destruction and enlargement or emphysema. ECM, extracellular matrix; MMP, matrix metalloproteinase.

The basic pathophysiological process in COPD consists of increased resistance to airflow, loss of elastic recoil and decreased expiratory flow rate. The alveolar walls frequently break because of the increased resistance of air flows. The hyper inflated lungs flatten the curvature of the diaphragm and enlarge the rib cage. The altered configuration of the chest cavity places the respiratory muscles, including the diaphragm, at a mechanical disadvantage and impairs their force

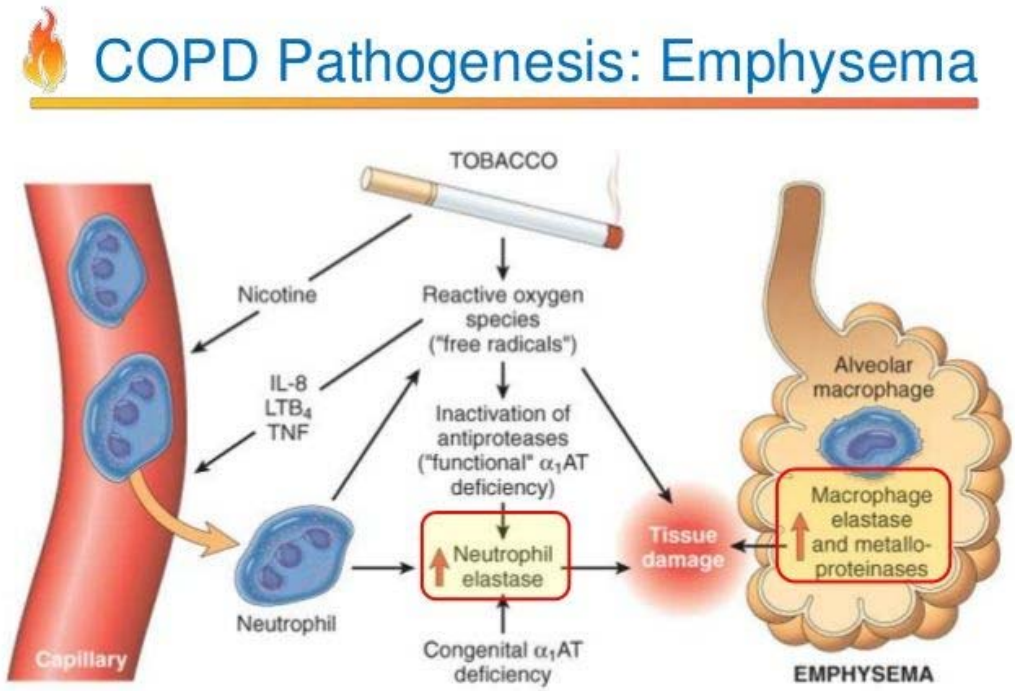
generating capacity. Consequently, the metabolic work of breathing increases and the sensation of dyspnea heightens.

Hogg has focused on the importance of *small airway obstruction*, most recently showing that airway remodelling and wall thickening, presence of inflammatory mucous exudates, and B cell and CD8 T cell inflammation are all associated with severity of COPD and progression of the disease.[39] Christie, Thurlbeck, and others have championed emphysema as the dominant pathology accounting for abnormal physiology, and have shown, for example, that in a subgroup of patients, the relationship between flow and recoil pressure is indeed normal. While many important insights came from this line of investigation, to this day we still do not understand the relative contribution of small airway obstruction versus emphysema in an individual patient, nor the potential relationship between these two lesions. This line of investigation is still fruitful, particularly with the ongoing revolution in imaging.

## THE ELASTASE: ANTIELASTASE HYPOTHESIS

Just over 40 years ago, two lines of evidence, one experimental and one clinical, suggested that emphysema is caused by destruction of elastic fibers by elastases. The first was by Laurell and Eriksson who, in 1963, described five patients with deficiency of α-1-AT, the primary inhibitor of the neutral serine proteinase neutrophil elastase (NE). Three of these five patients had emphysema.[40] The second came in 1965 when Gross and co-workers instilled papain into the lungs of rodents in an attempt to produce granulomas. Instead they found emphysema.[41]

Subsequently, investigators have instilled a variety of proteinases into animal lungs. Kuhn and colleagues[42], Senior and coworkers[43], Janoff and associates[44], and Snider and colleagues[45] were among the group of investigators who subsequently demonstrated that only elastolytic proteinases including pancreatic elastase and the more relevant human neutrophil elastase (HNE) caused emphysema. Hoidal's group showed that proteinase[46] also caused destructive lung disease. These seminal experiments formed the basis for the elastase : anti-elastase hypothesis, which states that the relative balance between elastases and their inhibitors determines the susceptibility of the lung to the destruction characteristic of emphysema.




**INFLAMMATION–EXTRACELLULAR MATRIX TURNOVER**

A classic study by Damiano and coworkers correlated the presence of HNE with COPD using immunogold staining.[47] However, other studies actually showed a negative correlation between emphysema and HNE or neutrophil number.[48,49] As discussed above, macrophages are abundant in COPD, yet the capacity of the macrophage to degrade elastin and hence contribute to disease pathogenesis was unproven until Senior and colleagues demonstrated that macrophages produce elastolytic matrix metalloproteinases[50,51] and Chapman and co-workers found elastolytic cysteine proteinases.[52]

Retamales and colleagues[53] found that even in end-stage lung disease, long after smoking cessation, there remains an exuberant inflammatory response. This suggests that the mechanisms of cigarette smoke–induced inflammation that initiate the disease differ from mechanisms that sustain inflammation after smoking cessation. Moreover, this study suggests that multiple inflammatory (and likely structural) cells interact to cause COPD, and that focusing on single cells and proteinases in isolation will not provide a comprehensive understanding of the disease process.

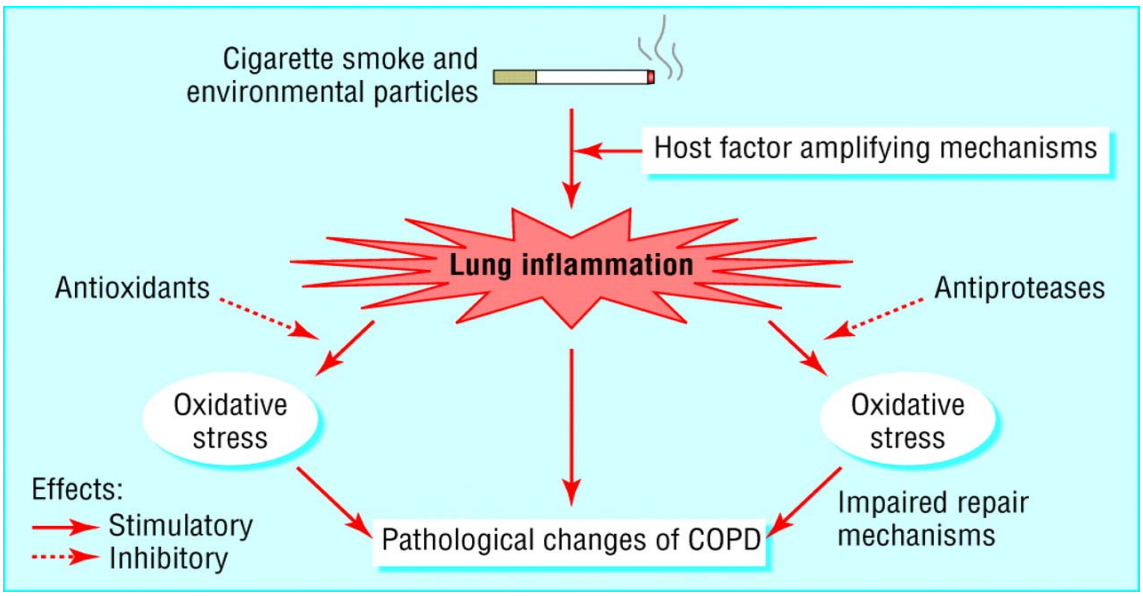
Cigarette smoke causes constitutive macrophages to produce MMP-12, which, in turn, cleaves elastin into fragments chemotactic for monocytes. This positive feedback loop perpetuates macrophage accumulation and lung destruction. The concept that proteolytically generated elastin fragments mediate monocyte chemotaxis was proven by Senior and co-workers[54] and Hunninghake and colleagues.[55] At the very least, this study demonstrates a critical role for macrophages in the development of emphysema and unmasks a proteinase dependent mechanism of inflammatory cell recruitment.

Of note, last year Grumelli and coworkers found that human CD8+ T cells derived from patients with COPD generate interferon (IFN)-γ–inducible chemokines that also function to upregulate expression of human macrophage MMP-12.[56] Studies by Churg and co-workers demonstrate that acute neutrophil

inflammation secondary to smoking is related to MMP-12–dependent tumor necrosis factor (TNF) shedding.[57]

## OXIDANT–ANTIOXIDANT BALANCE

Cigarette smoke and inflammatory cells have the capacity to produce reactive oxygen species, and they have been postulated to play a variety of roles in the pathogenesis of emphysema. One intriguing finding was that cigarette smoke can oxidize a methionine residue in the reactive center of A1PI, inactivating A1PI and thus altering the elastase : anti-elastase balance. Oxidants cannot degrade extracellular matrix but might modify elastin, making it more susceptible to proteolytic cleavage.



Recently, Barnes and colleagues have found that cigarette smoke oxidizes and inactivates histone deacetylase 2 (HDAC2), which acts to counter histone acetylase (HAT).[58] Acetylation of histone unwinds chromatin, allowing transcriptional complexes to bind to DNA. Thus, in the absence of HDAC2, RNA polymerase II and NF-kβ form a proinflammatory transcription complex. Finally, reactive oxygen species may also promote apoptosis of structural cells, a recent concept for initiation of emphysema.

**APOPTOSIS**

Kasahara and colleagues found that exposure to agents that initiate endothelial cell death (via VEGFRII inhibition) leads to non inflammatory airspace enlargement.[59] Nagai and co-workers then found that epithelial cell death (via caspase 3 delivery) also causes emphysema.[60] As mentioned above, the loss of an acinar unit results from the destruction of both the extracellular matrix (ECM) and the structural cells. These models suggest that death of structural cells may be an initiating event, with subsequent release of matrix-degrading proteinases. Whether this occurs in human COPD as a primary event is uncertain.

**INEFFECTIVE REPAIR**

The ability of the adult lung to repair damaged alveoli appears limited. In fact, as this study define genetic predisposition to COPD, this study speculate that smoking routinely leads to inflammation and lung damage, and those at risk lack

the capacity to repair this damage. In emphysema, aberrant alveolar and extracellular matrix repair results in coalesced and enlarged airspaces with depleted and disordered parenchymal elastic fibers, and excess and abnormally arranged collagen.

**SPIROMETRIC CLASSIFICATION OF COPD SEVERITY**

The present widely accepted classification of COPD is mainly based on the $FEV_1$ values1. It is as follows:

**Stage I :** **Mild COPD:** Characterized by mild airflow limitation ($FEV_1/FVC<0.70$; $FEV_1 \geq 80\%$ predicted). Symptoms of chronic cough and sputum production may be present. Patients are usually unaware of the illness.

**Stage II :** **Moderate COPD:** Characterized by worsening airflow limitation ($FEV_1/FVC < 0.70$; $50\% \leq FEV_1 < 80\%$ predicted), with shortness of breath typically developing on exertion with or without cough and sputum production. This is the stage at which patients typically seek medical attention.

**Stage III :** **Severe COPD:** Characterized by further worsening of airflow limitation ($FEV_1/FVC < 0.70$; $30\% \leq FEV_1 < 50\%$ predicted), greater shortness of breath, reduced exercise capacity, fatigue, and

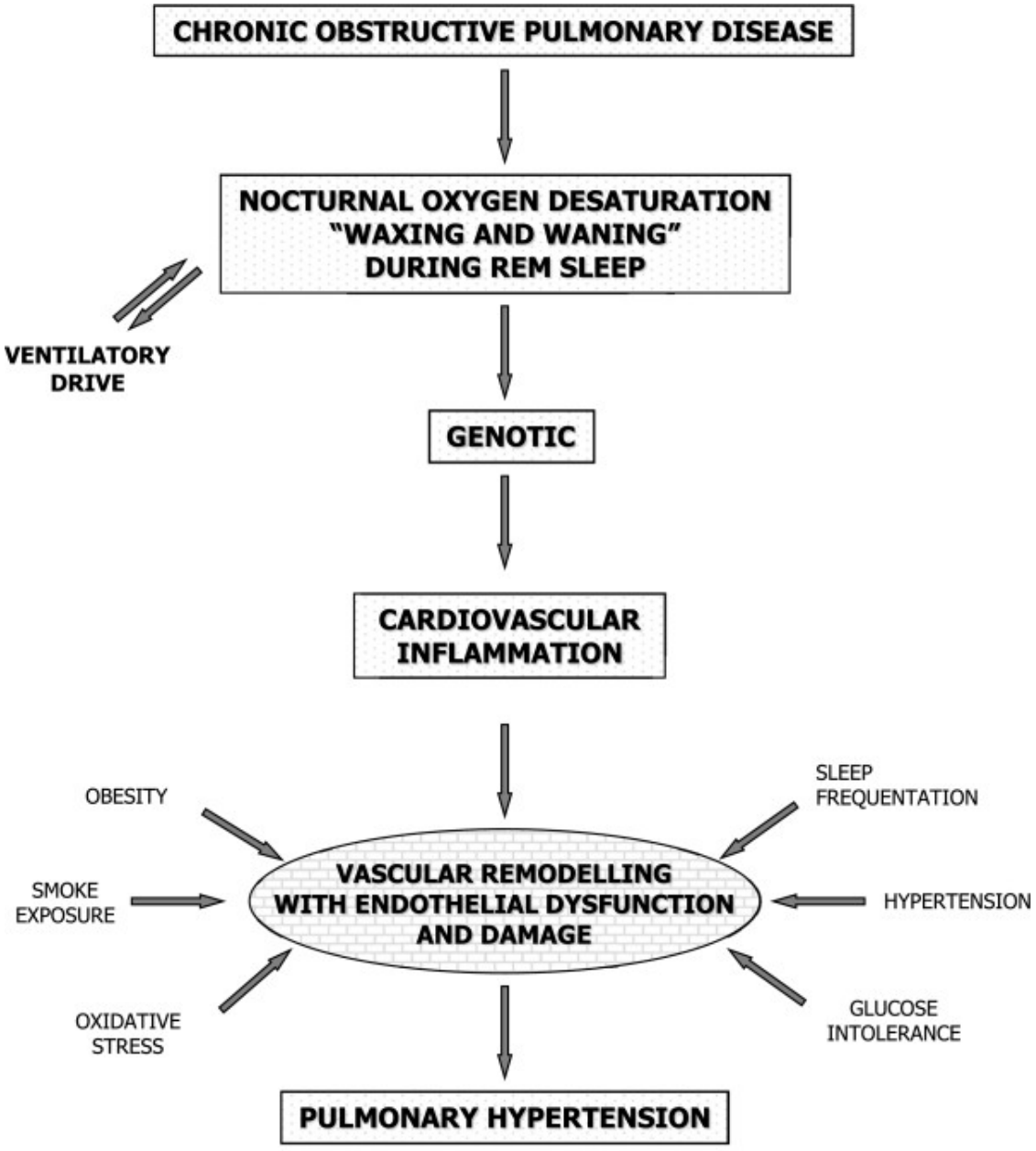
repeated exacerbations that almost always have an impact on patients' quality of life.

**Stage IV :** **Very Severe COPD:** Characterized by severe airflow limitation ($FEV_1/FVC < 0.70$; $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus the presence of chronic respiratory failure). Respiratory failure is defined as arterial partial pressure of oxygen ($PaO_2$) less than 8.0 kPa (60 mmHg) with or without arterial partial pressure of $CO_2$ ($PaCO_2$) greater than 6.7 kPa (50 mmHg) while breathing air at sea level.

| STAGE | SEVERITY | FEV1 |
|---|---|---|
| **I** | Mild | FEV1/FVC <0.70<br>FEV1 ≥ 80% predicted |
| **II** | Moderate | FEV1/FVC <0.70<br>50% ≤ FEV1 <80% predicted |
| **III** | Severe | FEV1/FVC <0.70<br>30% ≤ FEV1 <50% predicted |
| **IV** | Very Severe | FEV1/FVC <0.70<br>FEV1 <30% predicted or FEV1 <50% predicted plus chronic respiratory failure |

## LIMITATIONS OF SPIROMETRIC CLASSIFICATION

The spirometric classification, though good in many ways is not full proof for the assessment of severity of COPD. The $FEV_1$ is essential for the diagnosis and quantification of the respiratory impairment resulting from COPD.[61-63] In addition, the rate of decline in $FEV_1$ is a good marker of disease progression and mortality.[64,65]. However, the $FEV_1$ does not adequately reflect all the systemic manifestations of the disease. For example, the $FEV_1$ correlates weakly with the degree of dyspnea[66], and the change in $FEV_1$ does not reflect the rate of decline in patients' health.[67] More important, prospective observational studies of patients with COPD have found that the degree of dyspnea[68] and health-status scores[69] are more accurate predictors of the risk of death than is the $FEV_1$. Thus, although the $FEV_1$ is important to obtain and essential in the staging of disease in any patient with COPD, it alone as the sole parameter of severity does not throw light on the systemic involvement and progression of the disease.


CHRONIC OBSTRUCTIVE PULMONARY DISEASE
NOCTURNAL OXYGEN DESATURATION "WAXING AND WANING" DURING REM SLEEP
VENTILATORY DRIVE
GENOTIC
CARDIOVASCULAR INFLAMMATION
OBESITY
SLEEP FREQUENTATION
SMOKE EXPOSURE
VASCULAR REMODELLING WITH ENDOTHELIAL DYSFUNCTION AND DAMAGE
HYPERTENSION
OXIDATIVE STRESS
GLUCOSE INTOLERANCE
PULMONARY HYPERTENSION

## BODE INDEX

Due to reasons above stated, researchers described a new index – BODE index, for the comprehensive evaluation of patients with COPD. This multisystem grading index has four variables:

- Body mass index
- Obstruction to airflow ($FEV_1$)
- Dyspnea (MMRC dyspnea scale)
- Effort tolerance (6 minute walk test)

Each variable in the index correlates independently with the prognosis of COPD, is easily measurable, and serves as a surrogate for other potentially important variables. It is likely that they share some common underlying physiological determinants, but the distance walked in six minutes contains a degree of sensitivity not provided by the body mass index. The six-minute walk test is simple to perform and has been standardized.[70]

The body-mass index was also an independent predictor of the risk of death and was therefore included in the BODE index. This study evaluated the independent prognostic power of body-mass index in our cohort using different thresholds and found that values below 21 were associated with an increased risk of death, an observation similar to that reported by Landbo and co-workers in a large population study.[71]

The Global Initiative for Chronic Obstructive Lung Disease and the American Thoracic Society recommend that a patient's perception of dyspnea be included in any new staging system for COPD. Dyspnea represents the most disabling symptom of COPD; the degree of dyspnea provides information regarding the patient's perception of illness and can be measured. The MMRC dyspnea scale is simple to administer and correlates with other dyspnea scales and with scores of health status.[72] Furthermore, in a large cohort of prospectively followed patients with COPD, which used the threshold values included in the BODE index, the score on the MMRC dyspnea scale was a better predictor of the risk of death than was the $FEV_1$.

The BODE index combines the four variables by means of a simple scale. Weighing the variables included in the index did not improve the predictive power of the BODE index. Most likely, it failed to do so, because each variable included has already proved to be a good predictor of the outcome of COPD.

**PULMONARY HYPERTENSION:**

Pulmonary hypertension (PH) is defined by a mean pulmonary artery pressure ≥25 mm Hg at rest, measured during right heart catheterization.

Normal pulmonary artery pressure as follows:

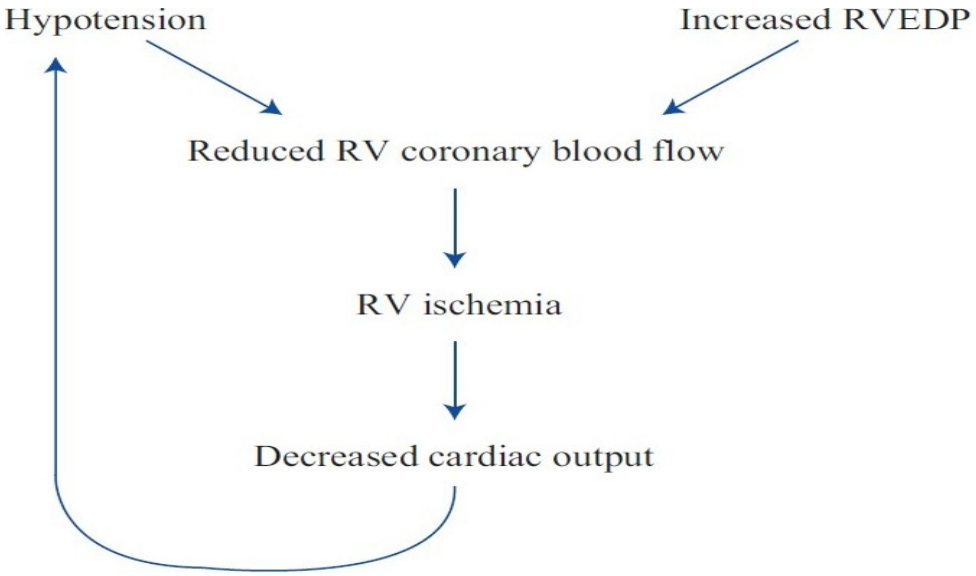
- Systolic pressure = 15 – 25mmhg
- Diastolic pressure = 5 – 10 mmhg

- Mean pressure = 10 – 15 mmhg

  Pulmonary Hypertension is present when the PASP is >30mmhg and the PAMP is >20mmhg.

**Basic Mechanism for PHT:**

1. Genetic and environmental factors.
2. Increased pulmonary blood flow.
3. Pulmonary vascular resistance.
4. Left side heart resistance to blood flow.




**Clinical features of PHT:**

SYMPTOMS: Cough, Chest pain, Breathlessness and Hemoptysis.

SIGNS: Loud $P_2$, TR Murmur, RVH and finally the features of RV failure.

**Mechanism of PHT formation in COPD:**

Pulmonary vascular remodelling in COPD is the main cause of increase in pulmonary artery pressure and is thought to result from the combined effects of hypoxia, inflammation and loss of capillaries in severe emphysema.

**Table 1: Classification Pulmonary Hypertension**

| | |
|---|---|
| Group 1 | Pulmonary Arterial Hypertension |
| Group 2 | PH from left-sided heart disease |
| Group 3 | PH from chronic hypoxic lung disease |
| Group 4 | PH from chronic blood clots |
| Group 5 | Unclear multifactorial mechanisms (sarcoidosis, hematological disorders, etc) |

**Investigations:**

1. Chest X-Ray
2. Ventilation – perfusion lung scan
3. CT pulmonary angiogram (CTPA)
4. ECG
5. Transthoracic / Transthoracic Echocardiogram
6. Pulmonary Function Test (PFT)
7. Arterial Blood Gas analysis (ABG)
8. CT Chest
9. Right heart cathetherisation

10. MRI chest

11. Radionuclide ventriculography

12. Lung Biopsy

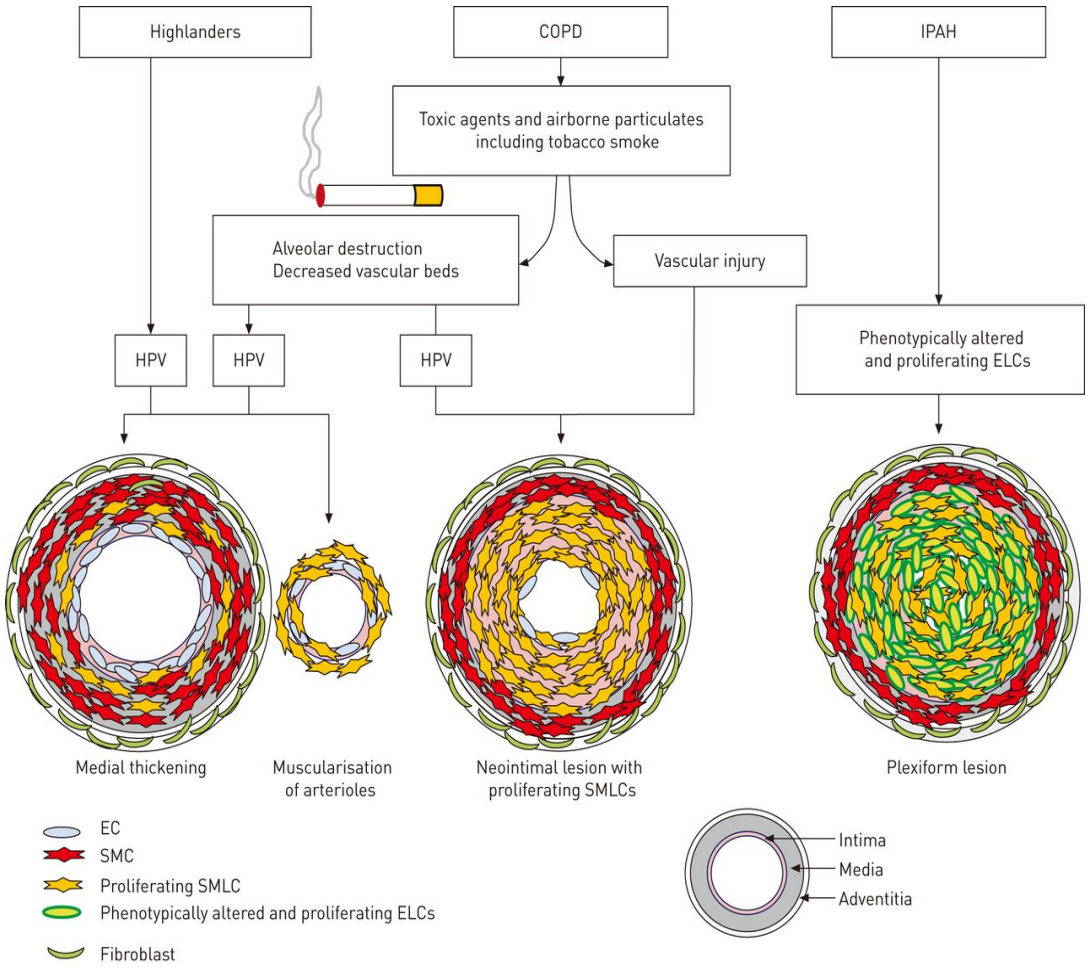
13. Nocturnal oximetry

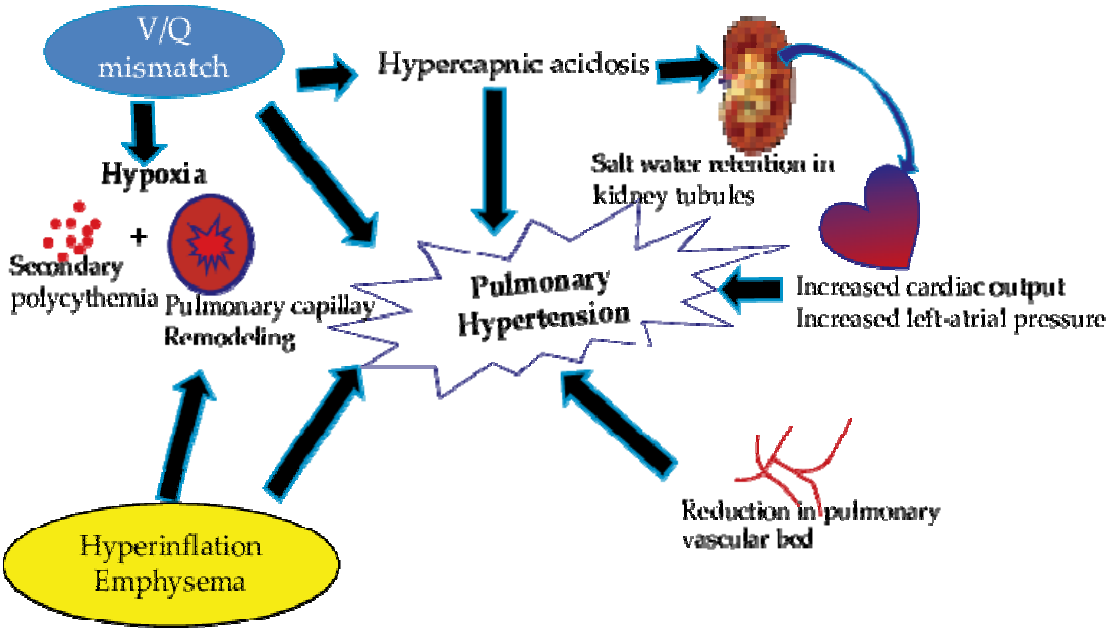
14. Routine Blood investigations

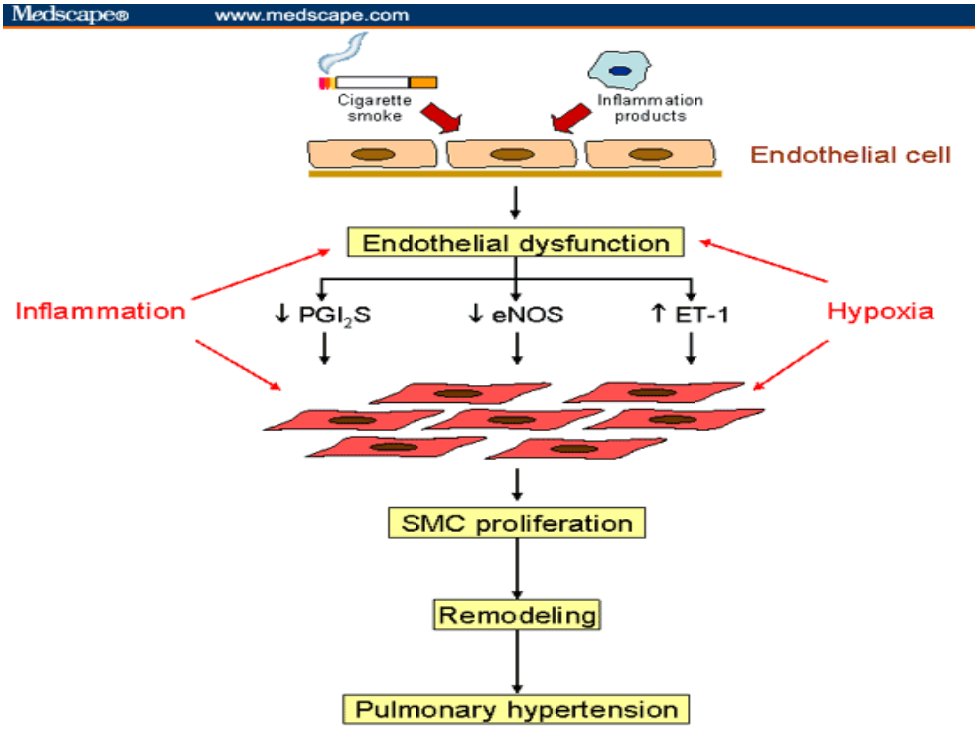
15. Contrast enhanced spiral chest CT

16. MR angiography

**PULMONARY VASCULATURE IN COPD**




V/Q mismatch
Hypercapnic acidosis
Hypoxia
Salt water retention in kidney tubules
Secondary polycythemia
+
Pulmonary capillay Remodeling
Pulmonary Hypertension
Increased cardiac output
Increased left-atrial pressure
Hyperinflation Emphysema
Reduction in pulmonary vascular bed

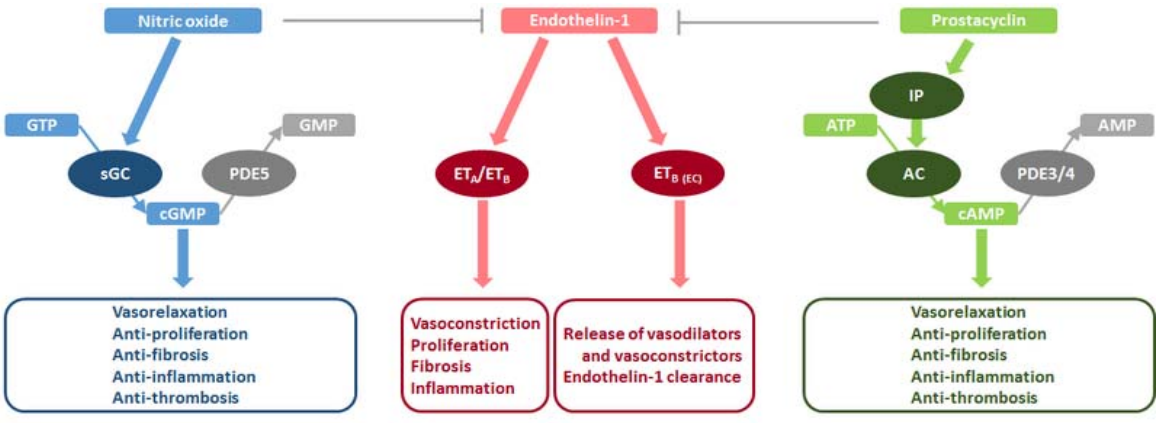

Medscape®
www.medscape.com
Cigarette smoke
Inflammation products
Endothelial cell
Endothelial dysfunction
Inflammation
↓ PGI2S
↓ eNOS
↑ ET-1
Hypoxia
SMC proliferation
Remodeling
Pulmonary hypertension

## GRADING OF PULMONARY HYPERTENSION:

| | Grading of pulmonary arterial hypertension* | | |
|---|---|---|---|
| | Systolic | Diastolic | Mean |
| **Grade 1** (Mild) | 30-50 | 20-25 | >30 |
| **Grade 2** (Moderate) | 50-70 | 26-35 | >40 |
| **Grade 3** (severe) | 70-110 | 36-45 | >50 |
| **Grade 4** (Systemic or supra systemic) | >110 | 46-55 | >60 |

*Data from 100 patients of PAH and rheumatic heart disease. Quintile 1 & 2 (Grade 1) qunitile 3 & 4 (Grade 2) quintile 5 (Grade 3) top 3%(Grade 4)

## MOLECULAR PATHOGENESIS OF PULMONARY HYPERTENSION IN COPD:




AC, adenylate cyclase; AMP, adenosine monophosphate; ATP, adenosine triphosphate; cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophosphate; EC, endothelial cells; $ET_A$, endothelin receptor A, $ET_B$, endothelin receptor B; GMP, guanosine monophosphate; GTP, guanosine triphosphate; IP, prostaglandin I receptor; PDE, phosphodiesterase; sGC, soluble guanylate cyclase

**Management of Pulmonary Hypertension:**

- ❖ Treat the underlying cause
- ❖ Correct hypoxaemia with oxygen
- ❖ Diuretics in RV failure

**Three pathways for the treatment of PHT:**

1. Nitric oxide – soluble guanyl cyclase pathway
2. Endothelin pathway
3. Prostacyclin pathway

**Role of surgery in PHT:**

- ♦ Atrial septostomy
- ♦ Heart – Lung transplantation
- ♦ Surgical intervention in pulmonary thromboembolism
- ♦ Lung transplantation

**Radiological findings in COPD:**

1. Hyperinflated lung fields
2. Low flat diaphragm
3. Long tubular heart shadow
4. Hyperlucent lung fields
5. Horizontal ribs

6. Widened intercostals spaces
7. Roomy apex
8. Bullae

**Chronic Bronchitis:**

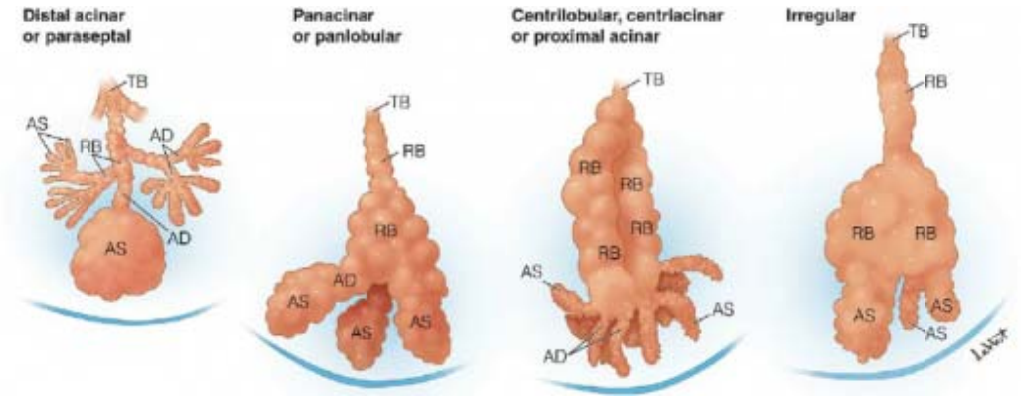
Chronic bronchitis is defined as defined as cough and sputum production on most days for atleast 3 consecutive months and for atleast two consecutive years.

**Emphysema:**

Empyesema is defined as abnormal permanent dilatation / enlargement of airspaces distal to the terminal bronchioles, and accompanied by destruction of their walls and without any obvious fibrosis.

**Types of emphysema:**

1. Centriacinar
2. Panacinar
3. Distal acinar
4. Irregular




**Difference between Chronic bronchitis & Emphysema**

| FEATURES | CHRONIC BRONCHITIS | EMPHYSEMA |
|---|---|---|
| **DIAGNOSIS** | CLINICAL | PATHOLOGICAL |
| **APPEARANCE** | BLUE BLOATER | PINK PUFFER |
| **CYANOSIS** | PROMINENT | ABSENT |
| **HYPERINFLATION** | + | ++ |
| **DYSPNEA** | + | ++ |
| **COUGH** | ++ | + |
| **COR PULMONALE** | ++ | + |

Airflow obstruction is defined as

- FEV1 < 80% predicted
- Forced expiratory volume: Forced vital capacity (FEV1:FVC) < 70%

Extrapulmonary manifestations of COPD include impaired nutrition, weight loss and skeletal muscle dysfunction and increased prevalence of osteoporosis.

**Spirometric findings in COPD:**

i. FEV1 <80% predicted
ii. FEV1:FVC <70%
iii. Increased TLC, FRC and RV
iv. Decreased Vital capacity
v. Decreased TLCO

**Management of stable COPD:**

As follows:

A) General measures:

- Stop smoking
- Vaccination – Influenza & Pneumococcal pneumonia

B) Drug therapy:

- Mild COPD – short acting bronchodilators OR Anticholinergics
- Moderate COPD – Regular SABA + LABA OR Anticholinergics

- Severe COPD – SABA + LABA + OR Anticholinergics + ICS + Oral theophylline

**Indications of steroid therapy in COPD:**

- Severe disease (FEV1 <50%) with two or more exacerbations requiring antibiotics or PO steroids / Year : inhaled corticosteroids (ICS).
- Acute exacerbations of COPD – Prednisolone at a dosage of 30mg/day PO for 10days is recommended.

**Surgical treatment options for COPD:**

1. Bullectomy
2. Lung volume reduction surgery
3. Lung transplantation

**Management of Acute Exacerbations of COPD:**

Home Management:

- ✓ Increased bronchodilator therapy.
- ✓ Short course of steroids PO.
- ✓ Antibiotics if appropriate.

Hospitalization:

- ✓ Oxygen – low flow or low concentration of 24% to 28%.
- ✓ Bronchodilators – Nebulised SABA + Antichonergics

- ✓ Oral prednisolone 30mg/day for 10days.
- ✓ Antibiotics – Amoxycillin or Macrolides.
- ✓ Respiratory stimulant
- ✓ NIV – severe hypercapneic respiratory failure (pH <7.35)

**Indications for hospitalization:**

- Cyanosis
- Peripheral edema
- An altered mentation
- Comorbidity
- Social isolation
- Grade IV dyspnea

**Complications of COPD:**

- ❖ Pulmonary hypertension
- ❖ Cor pulmonale
- ❖ Respiratory failure
- ❖ Polycyethemia
- ❖ Pneumothorax
- ❖ Secondary infection

# METHODOLOGY

**SETTING**

Department of General Medicine, Government Kilpauk Medical College, Chennai.

**INSTITUTIONAL ETHICS COMMITTEE APPROVAL:** Obtained

**STUDY DESIGN**

To evaluate the BODE index as a predictor of severity and Pulmonary hypertension in Chronic Obstructive Pulmonary Disease patients, a cross-sectional study design was chosen.

**PERIOD OF STUDY:** FEBRUARY 2018 to SEPTEMBER 2018

**SAMPLE SIZE:**

Sample size is calculated using epi info app. Assuming a prevalence of severe PHT in COPD as 30%, sample size is calculated as 81 for a CI of 95%.

**STUDY POPULATION:**

All the patients, clinically diagnosed to have COPD from the department of medicine, Govt. Kilpauk medical college & hospital, Chennai during the period, will be included in the study.

**INCLUSION CRITERIA**

- Male patients with symptoms suggestive of COPD as diagnosed by spirometry in stable condition.

**EXCLUSION CRITERIA**

- Patients with acute exacerbation of COPD
- Spirometry proved Bronchial asthma.
- Recent myocardial infarction < 4months
- Unstable angina
- Congestive heart failure (NYHA class III or IV)
- Inability to perform spirometry or 6 minute walk test
- Other comorbid illness like CKD, Systemic Hypertension, Cancer, etc.
- Lung infection
- Pulmonary Tuberculosis (active & past)
- Interstitial Lung Diseases (ILD)
- Females
- Liver diseases
- Unrelated life threatening major illness

## STUDY PROTOCOL

COPD patients who attended our outpatient clinic / admitted as inpatient at the Govt.Kilpauk Medical College & hospital in the department of General Medicine were enrolled into the study. Of these, 81 patients who met the inclusion criteria were included in the study after getting informed consent from them.

The patients with the following diagnostic criteria (according to the GOLD guidelines) were defined as having COPD:

1. The presence of cough and sputum production for at least 3 months in each of the two consecutive years
2. Exertional dyspnoea
3. Physical examination showing:
    - Signs of airflow limitation like prolonged expiration and expiratory wheeze which is not fully reversible.
    - Signs of hyperinflation.
    - Spirometry showing post bronchodilator $FEV_1/FVC$ ratio < 0.70.

**TABLE 314-1 GOLD CRITERIA FOR SEVERITY OF AIRFLOW OBSTRUCTION IN COPD**

| GOLD Stage | Severity | Spirometry |
|---|---|---|
| I | Mild | $FEV_1/FVC < 0.7$ and $FEV_1 \geq 80\%$ predicted |
| II | Moderate | $FEV_1/FVC < 0.7$ and $FEV_1 \geq 50\%$ but $< 80\%$ predicted |
| III | Severe | $FEV_1/FVC < 0.7$ and $FEV_1 \geq 30\%$ but $< 50\%$ predicted |
| IV | Very severe | $FEV_1/FVC < 0.7$ and $FEV_1 < 30\%$ predicted |

***Abbreviations:*** COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Lung Disease.

The present analysis was restricted to male patients only, who met the acceptability and reliability criteria of the American Thoracic Society to improve the diagnostic accuracy as sex may be a confounding factor in many of the parameters assessed.

For each enrolled subject, detailed history of smoking, personal and family medical histories were obtained. On the day of enrollment, height and weight were measured twice during the examination. Weight was measured to the nearest 100 grams with bare foot. Height was measured to the nearest mm with the stadometer.

Body mass index (BMI) was calculated by the formula.

$$BMI = \text{Weight in Kgs} / (\text{Height in Ms})^2$$

Smoking Index was calculated by the formula.

Smoking Index = (No. of cigarettes smoked / day x years of smoking) / 20

Spirometry was performed with an equipment that met the American Thoracic society performance criteria, in each of the cases on enrollment into the study and 20 minutes following the administration of salbutamol nebulisation. To adjust for the height, sex, age and sex published prediction equations for forced expiratory volume in 1 second ($FEV_1$) and forced vital capacity (FVC) were used. $FEV_1$ and FVC were calculated. The procedure was repeated on 2 occasions and the average value was taken.

A detailed history of the dyspnea experienced by the patient was taken. MMRC dyspnea scale was used to score the patients dyspnea.

**MMRC Dyspnea scale**

Grade 0: No dyspnea / only on severe exertion.

Grade 1: Dyspnea on hurrying / walking up a hill.

Grade 2: Walks slower than normal at level/pause while walking on level ground.

Grade 3: Stops for breath after walking 100 yards/few mins on level ground.

Grade 4: Too breathless to leave the house/dyspnea on dressing.

**The Modified Medical Research Council (MMRC) Dyspnoea Scale**

| Grade of dyspnoea | Description |
|---|---|
| 0 | Not troubled by breathlessness except on strenuous exercise |
| 1 | Shortness of breath when hurrying on the level *or* walking up a slight hill |
| 2 | Walks slower than people of the same age on the level because of breathlessness *or* has to stop for breath when walking at own pace on the level |
| 3 | Stops for breath after walking about 100 m *or* after a few minutes on the level |
| 4 | Too breathless to leave the house *or* breathless when dressing or undressing |

Six minute walk test was performed twice with a gap of 30 minutes rest in between and the average was taken. Patients were asked to walk on a level ground for maximum possible distance within duration of 6 minutes. Periods of rest taken, was also included in the 6 minutes test period.

The BODE index was calculated for each patient using the body mass index, the threshold value of $FEV_1$, the distance walked in 6 min, and the score on the Modified Medical Research Council (MMRC) dyspnea scale. The patients received points ranging from 0 (lowest value) to 3 (maximal value). For body mass index the values were 0 (>21) or 1 (<21). The scores for FEV1 were 0 (more than or equal to 65%), 1 (50 – 64%), 2 (36 – 49%) and 3 (less than or equal to 35%). The 6 minute walk test scores were 0 (> 350 ms), 1 (250 – 350 ms), 2 (150 – 249 ms) and 3 (< 150 ms). The MMRC dyspnea class 0 and I were given 0 points, class II – 1 point, class III – 2 points and class IV – 3 points. The points for each variable were added, so that the BODE index ranged from 0 to 10 points in

each patient. The BODE score of 0 – 2 was taken as mild COPD. Scores between 3-5 was considered as moderate disease and those more than or equal to 6 was considered as severe COPD.

**BODE INDEX**

| **BODE score** | **0** | **1** | **2** | **3** |
|---|---|---|---|---|
| $FEV_1$ | ≥65% | 50 – 64% | 36 – 49% | ≤35% |
| 6 min walk test | >350ms | 250 – 349 ms | 150 – 249 ms | <149 ms |
| Dyspnea scale | 0 – 1 | 2 | 3 | 4 |
| BMI | >21kg/$m^2$ | <21 kg/$m^2$ | | |

- Mild COPD (0 – 2)
- Moderate COPD (3 – 5)
- Severe COPD (≥ 6)

A standard 12 lead ECG was taken for each of the individual patients. QRS axis was determined by plotting the QRS potentials on a graph with lead I as X axis and aVF as Y axis. – 30 to + 90 was considered as normal axis, – 30º to – 90º as left axis , +90º to +180º as right axis and – 90º to + 180º was considered as north west axis. Echo cardiography was performed using 2D echo in the department of cardiology, Govt.Kilpauk Medical College. Ejection fraction and pulmonary pressure gradient was assessed. Pulmonary artery hypertension was graded as mild, moderate and severe.

Hemoglobin estimation was performed according to the routine standards using an automated analyzer at the biochemistry lab attached to the department of Biochemistry, Govt.Kilpauk Medical College.

A detailed history regarding number of exacerbations in the last two years was obtained from the patients response to the question “how many times you have been visited hospital in the past 2 years due to reasons related to COPD?”.

**FINANCIAL SUPPORT:** Nil

**CONFLICT OF INTEREST:** Nil

## STATISTICAL ANALYSIS

Statistical analysis was carried out in all the 81 patients after categorizing the variable. Baseline data was collected from patients with mild, moderate and severe COPD. Age, Body Mass Index (BMI), number of exacerbations, mean hemoglobin concentration, QRS axis, pulmonary hypertension in 2D Echo of all subjects were the parameters analyzed. BODE score is calculated with all the available data.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant in the multivariate analysis the one way ANOVA with Tukey's Post-Hoc test was used. To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value 0.05 is considered as significant level.

Statistical analysis was carried out using the standard formula. Microsoft excel 2007 and SPSS (statistical package for social sciences) version 23 software was used for data entry and analysis.

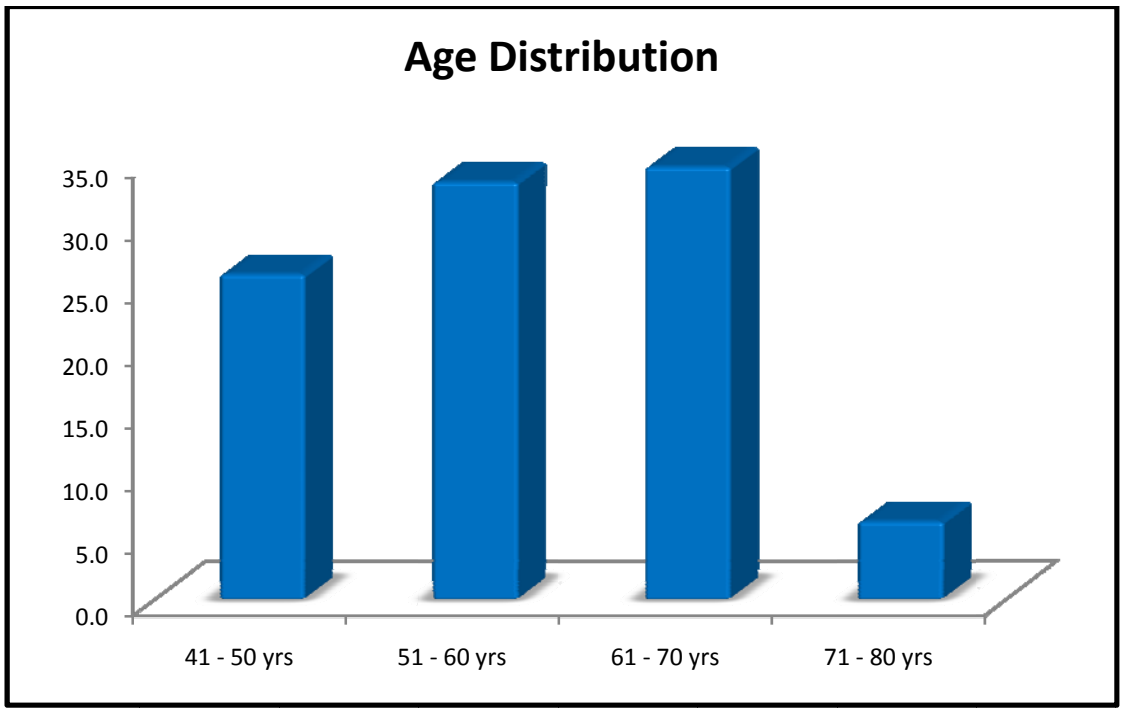
# RESULTS AND OBSERVATIONS

A total of 81 patients with COPD were enrolled in the study. All 81 patients were males. Among the patients with COPD, 21 (25.9%), 27 (33.3%), 28 (34.6%) and 5 (62%) belongs to age 41 – 50years, 51 – 60 years, 61 – 70years and 71 – 80 years respectively. Most patients are in the age group of 51 – 70 years as shown in Table 1 and Fig 1.

**Table 1: Age wise distribution in years**

| AGE | | | |
|---|---|---|---|
| | | Frequency | Percent |
| Valid | 41 - 50 yrs | 21 | 25.9 |
| | 51 - 60 yrs | 27 | 33.3 |
| | 61 - 70 yrs | 28 | 34.6 |
| | 71 - 80 yrs | 5 | 6.2 |
| | Total | 81 | 100.0 |

**Figure 1: Age wise distribution in years**



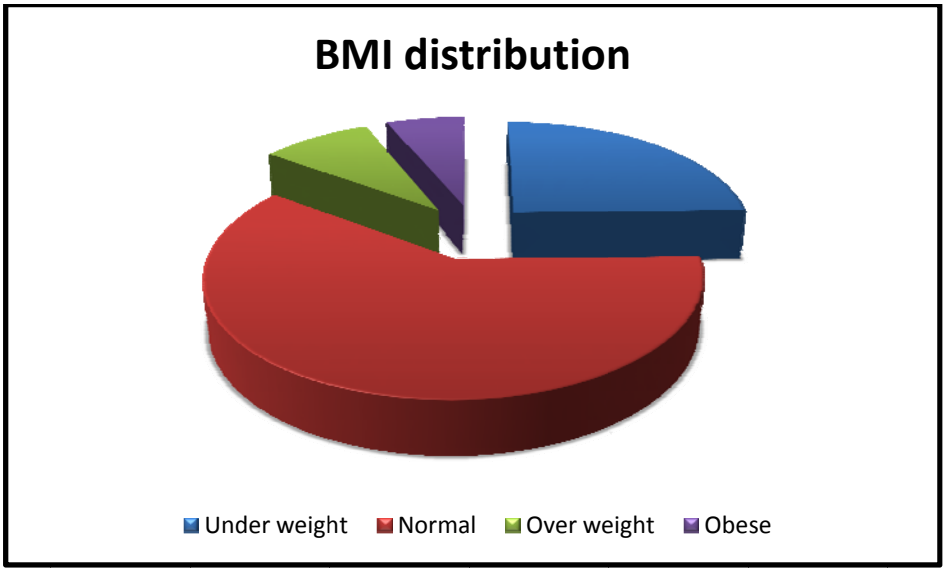

**BODY MASS INDEX (BMI):**

Among 81 patients, 20 (24.7%), 49 (60.5%), 7 (8.6%) and 5 (6.2%) belongs to Underweight, Normal, Overweight and Obese categories based on their BMI which is shown in Table 2 and Fig 2 below.

**Table 2: Body Mass Index (BMI) distribution**

| BMI | | | |
|---|---|---|---|
| | | Frequency | Percent |
| Valid | Under weight | 20 | 24.7 |
| | Normal | 49 | 60.5 |
| | Over weight | 7 | 8.6 |
| | Obese | 5 | 6.2 |
| | Total | 81 | 100.0 |

**Figure 2: Body Mass Index (BMI) distribution**



**BODY MASS INDEX (BMI) AND SEVERITY OF COPD:**

On analysing the distribution of BMI in relation to the severity of COPD categories, it was observed that the mean BMI were 21.34±3.78, 23.24±5.19and 20.64±2.89 in mild, moderate and severe category of COPD (p=0.121) as shown in Table 3 and Figure 3. The data subjected to ANOVA test reveals the existence of statistically non-significant association between BMI distribution and severity of COPD groups ($p > 0.05$).

**Figure 3: BMI with Severity of COPD correlation**

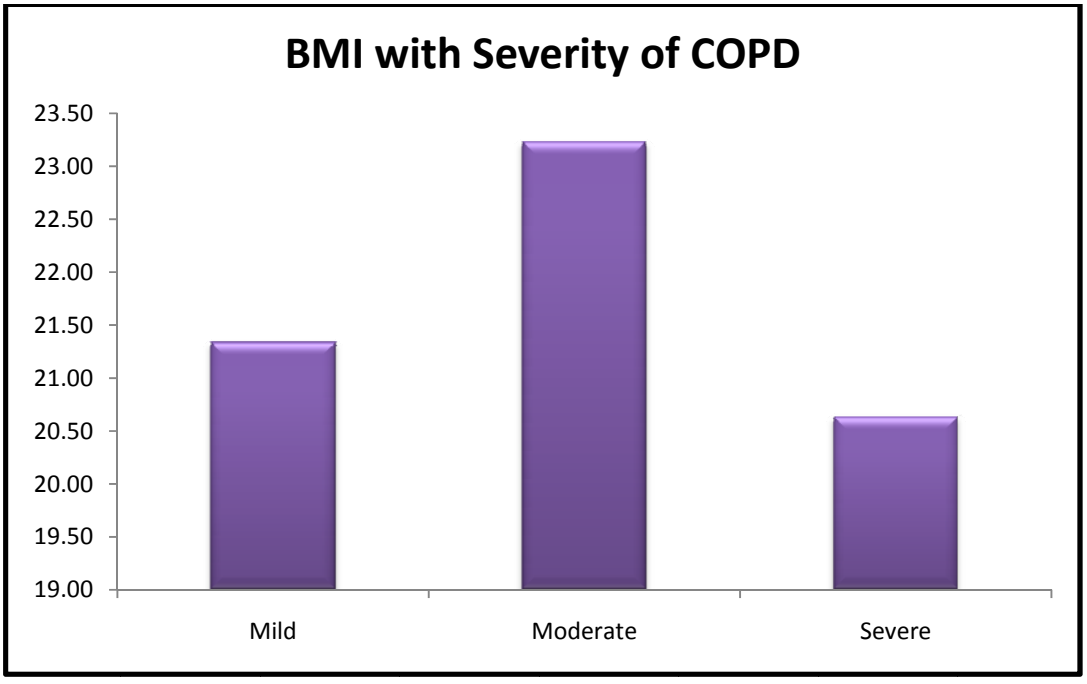


**Table 3: Correlation of BODE Score, BMI, No. of exacerbations and Hb(gms%) with severity of COPD**

| Descriptives | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Interval for Mean | | | |
| | | N | Mean | Std. Deviation | Std. Error | Lower Bound | Upper Bound | Minimum | Maximum |
| BODE score | Mild | 42 | .57 | .630 | .097 | .38 | .77 | 0 | 2 |
| | Moderate | 15 | 4.13 | .915 | .236 | 3.63 | 4.64 | 3 | 5 |
| | Severe | 24 | 8.00 | 1.251 | .255 | 7.47 | 8.53 | 6 | 10 |
| | Total | 81 | 3.43 | 3.384 | .376 | 2.68 | 4.18 | 0 | 10 |
| BMI | Mild | 42 | 21.34 | 3.78 | 0.58 | 20.17 | 22.52 | 15.05 | 30.99 |
| | Moderate | 15 | 23.24 | 5.19 | 1.34 | 20.36 | 26.11 | 16.70 | 32.04 |
| | Severe | 24 | 20.64 | 2.89 | 0.59 | 19.42 | 21.86 | 15.67 | 26.12 |
| | Total | 81 | 21.48 | 3.90 | 0.43 | 20.62 | 22.35 | 15.05 | 32.04 |
| No of Exacerbations | Mild | 42 | .62 | 1.147 | .177 | .26 | .98 | 0 | 5 |
| | Moderate | 15 | 5.53 | 1.959 | .506 | 4.45 | 6.62 | 4 | 12 |
| | Severe | 24 | 14.38 | 1.952 | .398 | 13.55 | 15.20 | 10 | 17 |
| | Total | 81 | 5.60 | 6.210 | .690 | 4.23 | 6.98 | 0 | 17 |
| Hb(gms%) | Mild | 42 | 10.907 | 1.4856 | .2292 | 10.444 | 11.370 | 7.7 | 14.0 |
| | Moderate | 15 | 8.740 | 1.0702 | .2763 | 8.147 | 9.333 | 7.5 | 11.1 |
| | Severe | 24 | 8.554 | 1.3394 | .2734 | 7.989 | 9.120 | 6.5 | 11.0 |
| | Total | 81 | 9.809 | 1.7796 | .1977 | 9.415 | 10.202 | 6.5 | 14.0 |

**Table 4: ANOVA Test for BODE score, BMI, No of Exacerbations and Hb(gms%) with severity of COPD**

| ANOVA | | | | | | |
|---|---|---|---|---|---|---|
| | | Sum of Squares | df | Mean Square | F | Sig. |
| BODE score | Between Groups | 851.857 | 2 | 425.929 | 518.946 | .0005 |
| | Within Groups | 64.019 | 78 | .821 | | |
| | Total | 915.877 | 80 | | | |
| BMI | Between Groups | 64.128 | 2 | 32.064 | 2.167 | .121 |
| | Within Groups | 1154.376 | 78 | 14.800 | | |
| | Total | 1218.504 | 80 | | | |
| No of Exacerbations | Between Groups | 2890.095 | 2 | 1445.047 | 577.240 | .0005 |
| | Within Groups | 195.263 | 78 | 2.503 | | |
| | Total | 3085.358 | 80 | | | |
| Hb(gms%) | Between Groups | 105.581 | 2 | 52.790 | 27.863 | .0005 |
| | Within Groups | 147.783 | 78 | 1.895 | | |
| | Total | 253.364 | 80 | | | |

**DISTRIBUTION OF SEVERITY OF COPD:**

Of the total 81 patients enrolled in the study, 42(51.9%) comes under Mild COPD, 15(18.5%) comes under Moderate COPD and 24(29.6%) comes under Severe COPD categories as shown in the table 5 and Figure 4.

**Table 5: Distribution of Severity of COPD patients**

| Severity of COPD | | | |
|---|---|---|---|
| | | Frequency | Percent |
| Valid | Mild | 42 | 51.9 |
| | Moderate | 15 | 18.5 |
| | Severe | 24 | 29.6 |
| | Total | 81 | 100.0 |

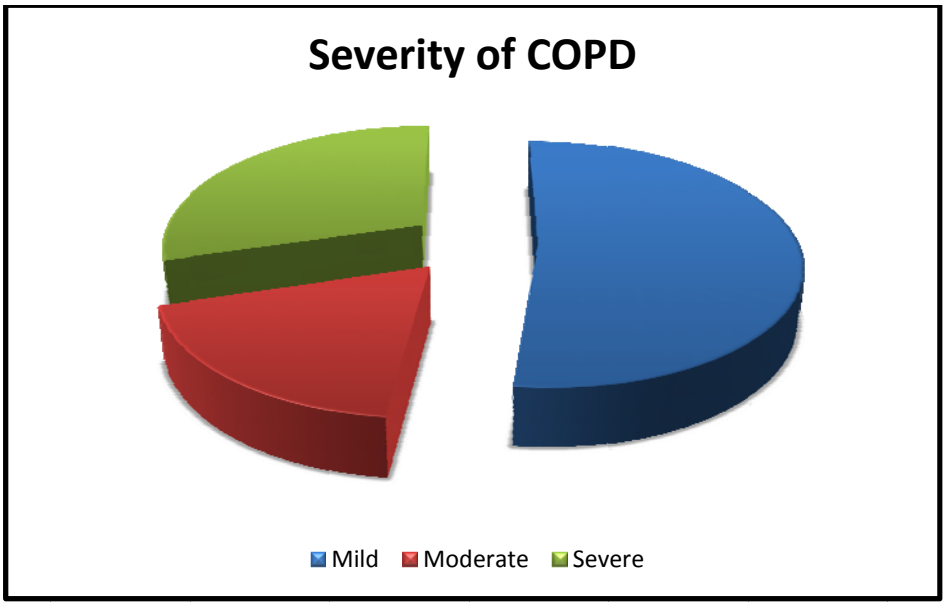



**Figure 4: Distribution of Severity of COPD**

**NUMBER OF EXACERBATIONS WITH SEVERITY OF COPD:**

On analysing the distribution of number of exacerbations in relation to the severity of COPD categories, it was observed that the mean number of exacerbations were 0.62±1.15, 5.53±1.96 and 14.38±1.95 in mild, moderate and severe category of COPD (p=0.0005) as shown in Table 3 and Figure 5. The data subjected to ANOVA test reveals the existence of statistically significant association between number of exacerbations distribution and severity of COPD groups ($p < 0.05$) as shown in Table 4.

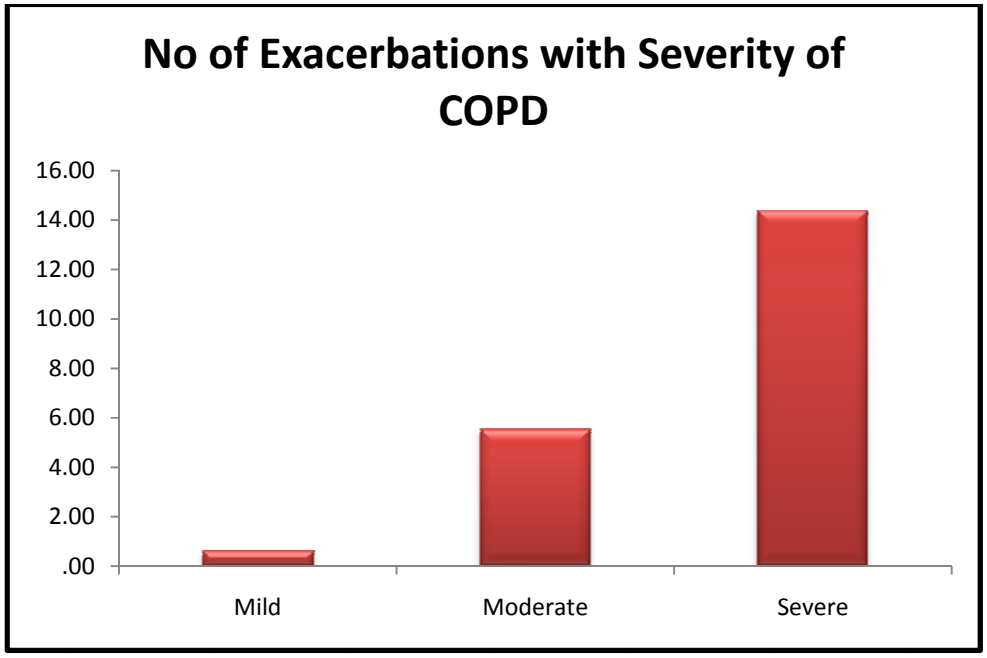



**Figure 5: Number of Exacerbations with Severity of COPD**

**HEMOGLOBIN AND SEVERITY OF COPD:**

On analysing the distribution of haemoglobin levels in relation to the severity of COPD categories, it was observed that the mean Hb levels were 10.91±1.49, 8.7±1.07 and 8.55.38±1.34 in mild, moderate and severe category of COPD (p=0.0005) as shown in Table 3 and Figure 6. The data subjected to ANOVA test reveals the existence of statistically significant association between haemoglobin levels and severity of COPD groups ($p < 0.05$) as shown in Table 4.

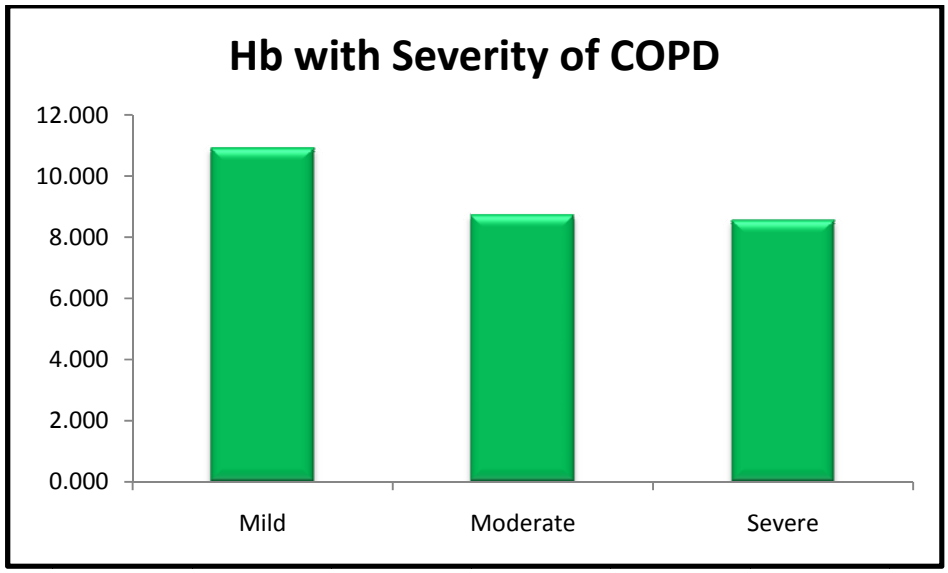



**Figure 6: Hemoglobin and Severity of COPD**

**ECG CHANGES IN COPD:**

Among 81 patients enrolled in the study, 53 (65.4%) patients had no changes in ECG but only 28 (34.6%) patients had ECG changes i.e 'P' Pulmonale and Right axis deviation (RAD) which is shown in the Table 7 and Figure 7.

**Table 6: Distribution of RAD & 'P' Pulmonale in COPD patients**

| P' Pumonale | | | |
|---|---|---|---|
| | | Frequency | Percent |
| Valid | N | 53 | 65.4 |
| | Y | 28 | 34.6 |
| | Total | 81 | 100.0 |

| RAD | | | |
|---|---|---|---|
| | | Frequency | Percent |
| Valid | N | 53 | 65.4 |
| | Y | 28 | 34.6 |
| | Total | 81 | 100.0 |

**Table 7: Distribution of ECG changes in COPD patients**

| ECG | | | |
|---|---|---|---|
| | | Frequency | Percent |
| Valid | No | 53 | 65.4 |
| | Yes | 28 | 34.6 |
| | Total | 81 | 100.0 |

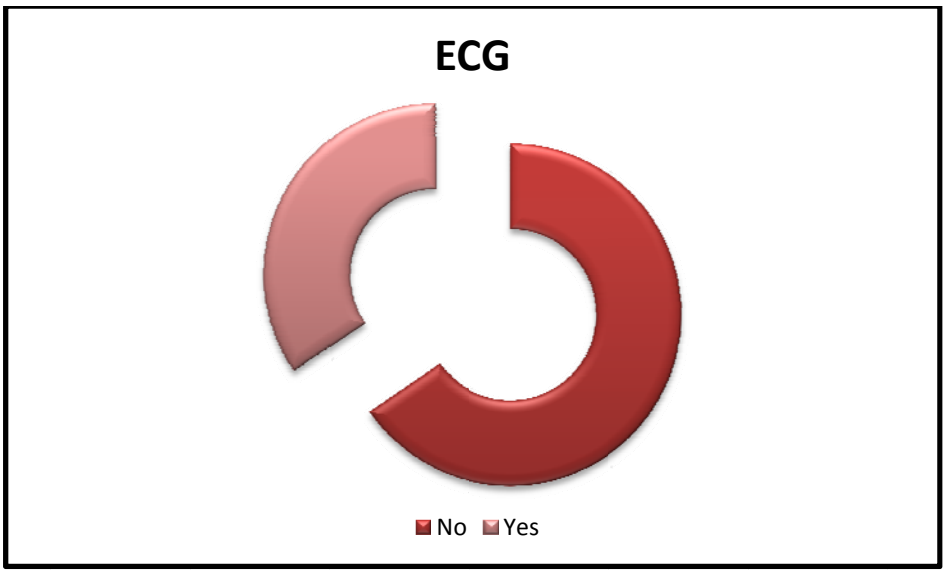



**Figure 7: Distribution of ECG changes in COPD patients**

**ECG CHANGES AND SEVERITY OF COPD:**

On cross tabulation of severity of COPD status in relation to the ECG changes, it was observed that the incidence of ECG changes was associated with 2.40% 0f mild category of COPD. 46.70% of moderate category of COPD and 83.30% of severe category of COPD. ($p=0.0005$) as shown in Table 8 and Figure 8. The data subjected to chi squared test reveals the existence of statistically significant association between severity of COPD status and ECG changes groups ($p < 0.05$) as shown in Table 8A.

**Table 8: ECG changes and Severity of COPD**

| ECG * Severity of COPD Crosstabulation | | | | | | |
|---|---|---|---|---|---|---|
| | | | Severity of COPD | | | |
| | | | Mild | Moderate | Severe | Total |
| ECG | N | Count | 41 | 8 | 4 | 53 |
| | | % | 97.6% | 53.3% | 16.7% | 65.4% |
| | Y | Count | 1 | 7 | 20 | 28 |
| | | % | 2.4% | 46.7% | 83.3% | 34.6% |
| Total | | Count | 42 | 15 | 24 | 81 |
| | | % | 100.0% | 100.0% | 100.0% | 100.0% |

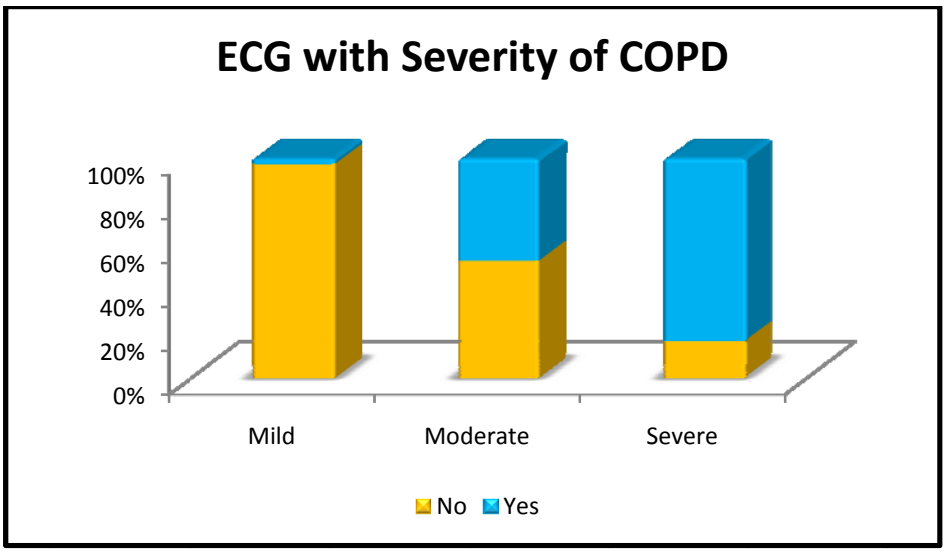



**Figure 8: ECG changes and Severity of COPD**

**Table 8A: Chi-Square tests for ECG Vs Severity of COPD**

| ECG VS Severity - Chi-Square Tests | | | |
|---|---|---|---|
| | Value | df | Asymp. Sig. (2-sided) |
| Pearson Chi-Square | 45.441[a] | 2 | .0005 |
| Likelihood Ratio | 52.640 | 2 | .000 |
| N of Valid Cases | 81 | | |

**ECG CHANGES AND PULMONARY HYPERTENSION:**

On cross tabulation of PHT status in relation to the ECG changes, it was observed that the incidence of ECG changes was associated with 0.00% 0f mild category of PHT, 50.00% of moderate PHT and 80.80% of severe PHT (p=0.0005) as shown in Table 9 and Figure 9. The data subjected to chi squared test reveals the existence of statistically significant association between PHT status and ECG changes groups ($p < 0.05$) as given by Table 10.

| ECG/PHT | Normal | Mild | Moderate | Severe |
|---|---|---|---|---|
| No | 100.0% | 100.0% | 50.0% | 19.2% |
| Yes | | | 50.0% | 80.8% |

**Table 7: ECG changes and PHT**

| ECG * PHT Crosstabulation | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | ECHO PHT | | | | Total |
| | | | Normal | Mild | Moderate | Severe | |
| ECG | N | Count | 11 | 30 | 7 | 5 | 53 |
| | | % | 100.0% | 100.0% | 50.0% | 19.2% | 65.4% |
| | Y | Count | 0 | 0 | 7 | 21 | 28 |
| | | % | 0.0% | 0.0% | 50.0% | 80.8% | 34.6% |
| Total | | Count | 11 | 30 | 14 | 26 | 81 |
| | | % | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

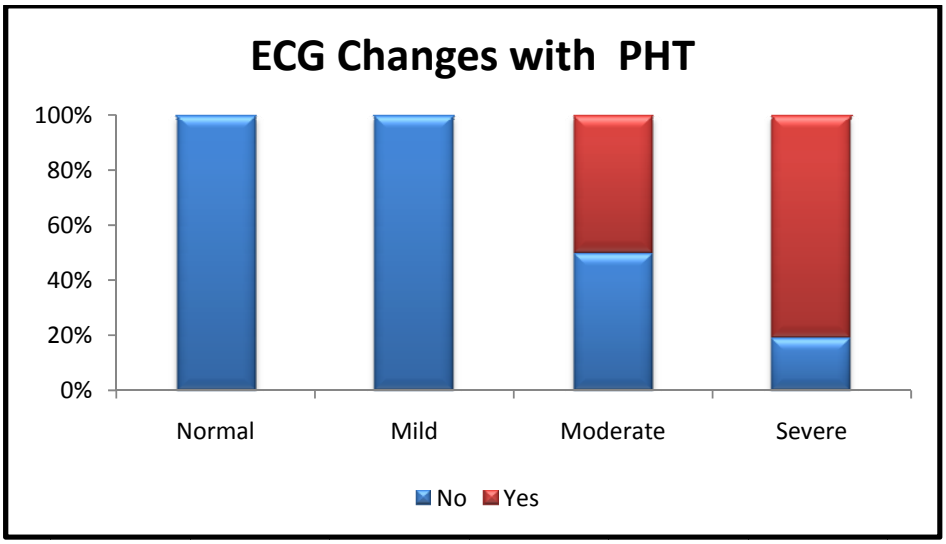



**Figure 9: ECG changes and PHT**

**Table 10: Chi Square Test for ECG changes and PHT**

| ECG Changes - Chi-Square Tests | | | |
|---|---|---|---|
| | Value | df | Asymp. Sig. (2-sided) |
| Pearson Chi-Square | 47.671[3] | 3 | .0005 |
| Likelihood Ratio | 59.582 | 3 | .000 |
| N of Valid Cases | 81 | | |

**PULMONARY HYPERTENSION (PHT):**

Among the 81 patients included in the study, 30(37%) had Mild PHT, 14(17.3%) had Moderate PHT, 26(32.1%) had Severe PHT and 11(13.6%) had no evidence of PHT in 2D ECHO as shown in Table 12 and Figure 10.

**Table 11: Distribution of COPD & PHT**

| | PHT | COPD |
|---|---|---|
| Mild | 37.0% | 51.9% |
| Moderate | 17.3% | 18.5% |
| Severe | 32.1% | 29.6% |
| No | 13.6% | |

**Table 12: Distribution of PHT**

| PHT | | | |
|---|---|---|---|
| | | Frequency | Percent |
| Valid | Mild | 30 | 37.0 |
| | Moderate | 14 | 17.3 |
| | Severe | 26 | 32.1 |
| | No | 11 | 13.6 |
| | Total | 81 | 100.0 |

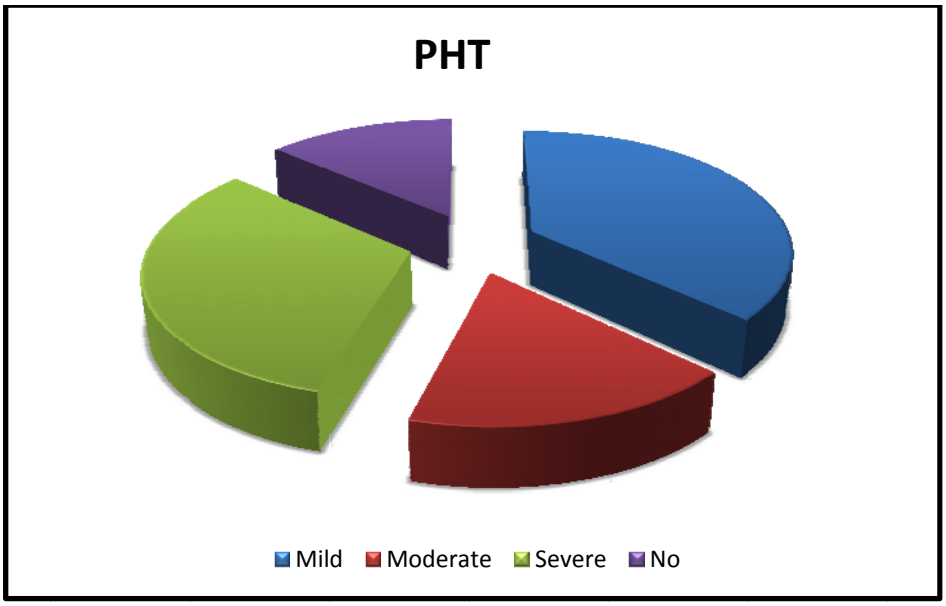



**Figure 10: Distribution of PHT**

**PULMONARY HYPERTENSION AND SEVERITY OF COPD:**

On cross tabulation of severity of COPD status in relation to the ECHO PHT categories, it was observed that the incidence of mild PHT was 37.00% and majority of it is associated with mild category of COPD (35.80%). Similarly the incidence of moderate PHT was 17.30% and majority of it is associated with moderate category of COPD (13.60%). Further looking into the incidence of severe PHT was 32.10% and majority of it is associated with severe category of COPD (27.20%). (p=0.0005) as shown in Table 10 and Figure 10. The data subjected to chi squared test reveals the existence of statistically significant association between severity of COPD status and PHT groups ($p < 0.05$) as shown by Table 14.

**Table 13: PHT and severity of COPD**

| PHT * Severity of COPD Crosstabulation | | | | | | |
|---|---|---|---|---|---|---|
| | | | Severity of COPD | | | Total |
| | | | Mild | Moderate | Severe | |
| ECHO PHT | Mild | Count | 29 | 0 | 1 | 30 |
| | | % | 35.8% | 0.0% | 1.2% | 37.0% |
| | Moderate | Count | 2 | 11 | 1 | 14 |
| | | % | 2.5% | 13.6% | 1.2% | 17.3% |
| | No | Count | 11 | 0 | 0 | 11 |
| | | % | 13.6% | 0.0% | 0.0% | 13.6% |
| | Severe | Count | 0 | 4 | 22 | 26 |
| | | % | 0.0% | 4.9% | 27.2% | 32.1% |
| Total | | Count | 42 | 15 | 24 | 81 |
| | | % | 51.9% | 18.5% | 29.6% | 100.0% |

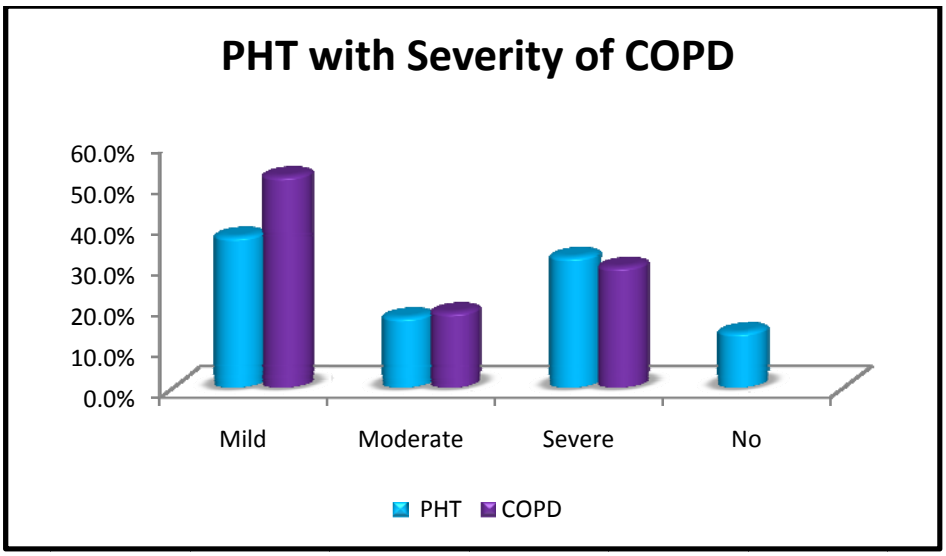



**Figure 11: PHT and Severity of COPD**

**Table 14: Chi Square test for PHT and Severity of COPD**

| PHT - Chi-Square Tests | | | |
|---|---|---|---|
| | Value | df | Asymp. Sig. (2-sided) |
| Pearson Chi-Square | 108.005[a] | 6 | .0005 |
| Likelihood Ratio | 114.688 | 6 | .000 |
| N of Valid Cases | 81 | | |

## CORRELATION OF BODE SCORE WITH PHT:

On analysing the distribution of BODE scores in relation to the PHT categories, it was observed that the mean BODE Scores were 1.00±1.29, 3.50±1.79 and 7.62±1.68 in mild, moderate and severe category of PHT (p=0.0005) as shown in Table 15 and Figure 12. The data subjected to ANOVA test reveals the existence of statistically significant association between BODE score distribution and severity of PHT groups ($p < 0.05$) as given by Table 16. Statiscal significance as shown by Post Hoc tests is given in Table 17.

**Table 15: BODE Score and PHT Correlation**

| Descriptives | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| BODE score | | | | | | | | |
| PHT | N | Mean | Std. Deviation | Std. Error | Interval for Mean | | Minimum | Maximum |
| | | | | | Lower Bound | Upper Bound | | |
| Normal | 11 | .09 | .302 | .091 | -.11 | .29 | 0 | 1 |
| Mild | 30 | 1.00 | 1.287 | .235 | .52 | 1.48 | 0 | 7 |
| Moderate | 14 | 3.50 | 1.787 | .478 | 2.47 | 4.53 | 0 | 6 |
| Severe | 26 | 7.62 | 1.675 | .329 | 6.94 | 8.29 | 4 | 10 |
| Total | 81 | 3.43 | 3.384 | .376 | 2.68 | 4.18 | 0 | 10 |

**Figure 12: BODE Score and PHT Correlation**

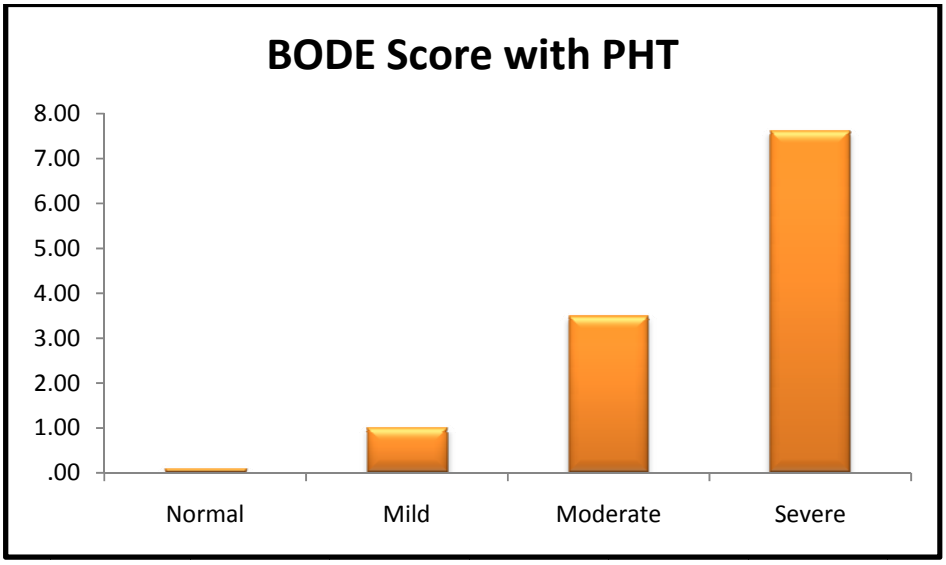



**Table 16: ANOVA Test for Correlation of BODE Score and PHT**

| ANOVA - BODE Score & PHT | | | | | |
|---|---|---|---|---|---|
| BODE score | | | | | |
| | Sum of Squares | df | Mean Square | F | Sig. |
| Between Groups | 755.314 | 3 | 251.771 | 120.740 | .0005 |
| Within Groups | 160.563 | 77 | 2.085 | | |
| Total | 915.877 | 80 | | | |

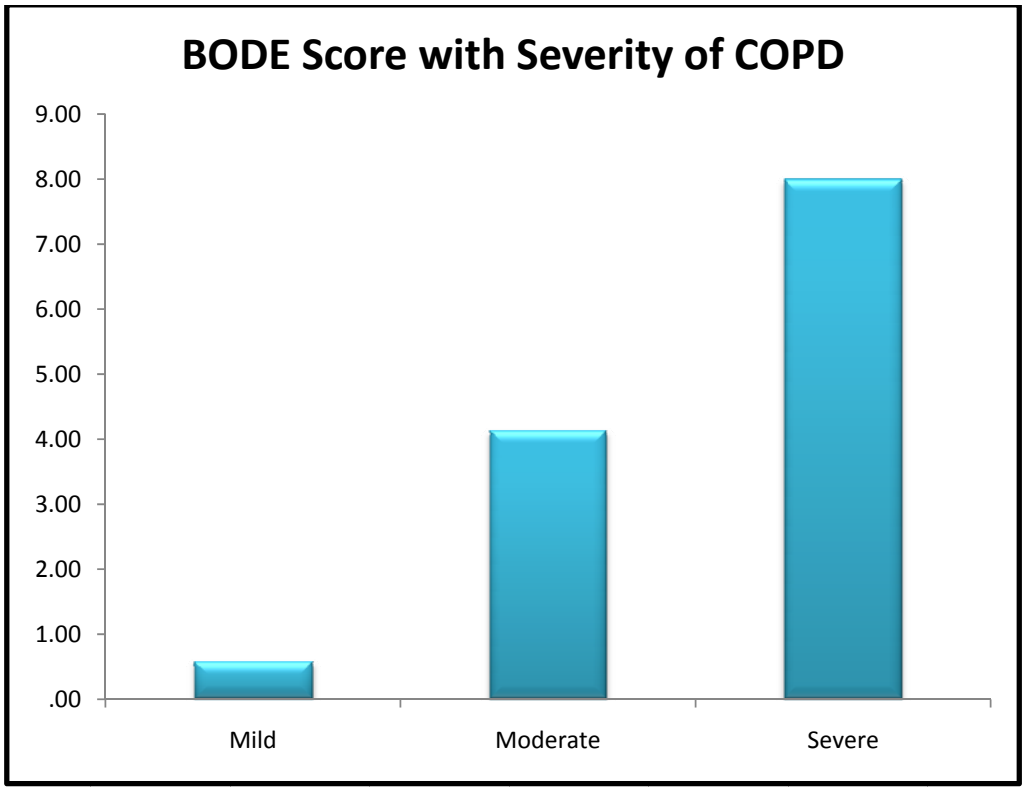
**Table 17: Post Hoc Test for correlation of BODE Score and PHT**

| Multiple Comparisons - Post Hoc Tests | | | | | | |
|---|---|---|---|---|---|---|
| Dependent Variable: BODE score | | | | | | |
| (I) PHT | | Mean Difference (I-J) | Std. Error | Sig. | Interval Lower Bound | Interval Upper Bound |
| Normal | Mild | -.909 | .509 | .288 | -2.25 | .43 |
| | Moderate | -3.409* | .582 | .0005 | -4.94 | -1.88 |
| | Severe | -7.524* | .519 | .0005 | -8.89 | -6.16 |
| Mild | Normal | .909 | .509 | .288 | -.43 | 2.25 |
| | Moderate | -2.500* | .467 | .0005 | -3.73 | -1.27 |
| | Severe | -6.615* | .387 | .0005 | -7.63 | -5.60 |
| Moderate | Normal | 3.409* | .582 | .000 | 1.88 | 4.94 |
| | Mild | 2.500* | .467 | .000 | 1.27 | 3.73 |
| | Severe | -4.115* | .479 | .0005 | -5.37 | -2.86 |
| Severe | Normal | 7.524* | .519 | .000 | 6.16 | 8.89 |
| | Mild | 6.615* | .387 | .000 | 5.60 | 7.63 |
| | Moderate | 4.115* | .479 | .000 | 2.86 | 5.37 |
| *. The mean difference is significant at the 0.05 level. | | | | | | |

**BODE SCORE AND SEVERITY OF COPD:**

On analysing the distribution of BODE score in relation to the severity of COPD categories, it was observed that the mean BODE Scores were 0.57±0.63, 4.13±0.92 and 8.00±1.25 in mild, moderate and severe category of COPD (p=0.0005) respectively as shown in Table 3 and Figure 13. The data subjected to ANOVA test reveals the existence of statistically significant association between BODE score distribution and severity of COPD groups ($p < 0.05$) as given by Table 4.

**Figure 13: BODE Score and its correlation with Severity of COPD**



## Table 16: Post Hoc Tests for Multiple Comparisons

| Post Hoc Tests – Multiple Comparisons | | | | | | | |
|---|---|---|---|---|---|---|---|
| Tukey HSD | | | | | | | |
| Dependent Variable | | | Mean Difference (I-J) | Std. Error | Sig. | Interval Lower Bound | Interval Upper Bound |
| BODE score | Mild | Moderate | -3.562* | .273 | .0005 | -4.21 | -2.91 |
| | | Severe | -7.429* | .232 | .0005 | -7.98 | -6.87 |
| | Moderate | Mild | 3.562* | .273 | .000 | 2.91 | 4.21 |
| | | Severe | -3.867* | .298 | .0005 | -4.58 | -3.15 |
| | Severe | Mild | 7.429* | .232 | .000 | 6.87 | 7.98 |
| | | Moderate | 3.867* | .298 | .000 | 3.15 | 4.58 |
| BMI | Mild | Moderate | -1.89314 | 1.15716 | .237 | -4.6579 | .8716 |
| | | Severe | .70661 | .98439 | .754 | -1.6454 | 3.0586 |
| | Moderate | Mild | 1.89314 | 1.15716 | .237 | -.8716 | 4.6579 |
| | | Severe | 2.59975 | 1.26622 | .107 | -.4256 | 5.6251 |
| | Severe | Mild | -.70661 | .98439 | .754 | -3.0586 | 1.6454 |
| | | Moderate | -2.59975 | 1.26622 | .107 | -5.6251 | .4256 |
| No of Exacerbations | Mild | Moderate | -4.914* | .476 | .0005 | -6.05 | -3.78 |
| | | Severe | -13.756* | .405 | .0005 | -14.72 | -12.79 |
| | Moderate | Mild | 4.914* | .476 | .000 | 3.78 | 6.05 |
| | | Severe | -8.842* | .521 | .0005 | -10.09 | -7.60 |
| | Severe | Mild | 13.756* | .405 | .000 | 12.79 | 14.72 |
| | | Moderate | 8.842* | .521 | .000 | 7.60 | 10.09 |
| Hb(gms%) | Mild | Moderate | 2.1671* | .4140 | .0005 | 1.178 | 3.156 |
| | | Severe | 2.3530* | .3522 | .0005 | 1.511 | 3.195 |
| | Moderate | Mild | -2.1671* | .4140 | .000 | -3.156 | -1.178 |
| | | Severe | .1858 | .4531 | .912 | -.897 | 1.268 |
| | Severe | Mild | -2.3530* | .3522 | .000 | -3.195 | -1.511 |
| | | Moderate | -.1858 | .4531 | .912 | -1.268 | .897 |

# DISCUSSION

COPD is predicted to be one of the most common killer lung disease affecting a large number of population by the year 2020. In the recent past, more resource has been utilized to formulate a simple and effective index for assessing the severity of COPD. Finally the researchers have found that BODE index would fulfill the necessity. But most of the research has been limited to finding the usefulness of the index in predicting the morbidity and mortality in patients with COPD. In our study we tried to evaluate the usage of this Index in predicting the severity of COPD in terms of number of exacerbations, Hemoglobin levels, Cardiac involvement by seeing the grade of pulmonary hypertension and correlations with many variables. The results which we got in our research would definitely bring a significant impact in the management of COPD in the near future.

Only male patients were included in our research, since males are more commonly affected in COPD. Hence, a uniform study group has thus been made. Such a selection would thus remove the gender related differences in Forced End expiratory Volume in 1 second, Body Mass Index (BMI) and patient perception of dyspnea.

Kian-chung etal[2] and Celli etal[5] has shown in their respective studies that BODE score increases with age. This study also shows a significant increase in the severe and moderately severe group. This could be due to the progression of COPD with age.

Studies by Celli etal[5] and Kian-Chung etal[2] has proven that grouping COPD patients into three groups with BODE scores 0 – 2 as first group, 3 – 5 as second and 6 or more as the third group correlates well with severity in terms of hospitalization and mortality. Hence we have accepted the same classification and grouped the above groups as mild, moderate and severe COPD.

In our study the distribution of mean BODE scores between the severity of COPD categories is meaningfully significant. This is evident by the decreased mean BODE score in mild category compared to moderate category (mean reduction difference of 3.56 score points, 86% lower) and decreased mean BODE score in moderate category compared to severe category (mean reduction difference of 3.87 score points, 48% lower) which is similar to the results of the study Celli etal[5] and Kian – Chung etal[2]. This proves that as the BODE Index Score increases the severity of COPD also increases and thus the mortality also increases.

Results from this study go along with most other studies, in the relationship of smoking to BODE index. Studies by Kian-chung etal[2], Celli etal[5], and Karoli etal[85] have all proven beyond doubt that higher duration of smoking is

associated with higher BODE index. The study revealed that there was significant increase in the BODE index in patients with a higher duration of smoking.

While considering BMI as a criteria for BODE index scoring, significance is only given to whether it is more, or less than 21. In our study we found that the BMI progressively declines with severity among the patients with COPD. Emil etal[4] had described the depletion of free fat mass and thereby a reduction in BMI in patients with COPD.

Arcasoy et al[87] has demonstrated an incidence of pulmonary hypertension of around 16 % in patients with COPD. Stevens et al[88] showed that the proportion of patients with pulmonary hypertension is higher among patients with severe COPD. Our study revealed a total incidence of 86.4 % of PAH among patients with COPD. The proportion was higher in the severe group with 1.2% having moderate PAH and 27.2% having severe PAH. In our study the distribution of severity of COPD status between the PHT categories is meaningfully significant. This is evident by the association of severity of COPD status in mild category compared to mild category of PHT is 97%, moderate level of severity of COPD to moderate PHT is 79% and severe level of severity of COPD to moderate PHT is 86% which implies that as the COPD severity increases the severity of cardiac involvement also increases.

In our study the distribution of mean BODE scores between the PHT categories is meaningfully significant. This is evident by the decreased mean BODE score in mild category compared to moderate category (mean reduction difference of 2.50 score points, 71% lower) and decreased mean BODE score in moderate category compared to severe category (mean reduction difference of 4.12 score points, 54% lower). Hence, as the BODE Index score increases the Severity of Pulmonary hypertension also increases.

Burch et al[65] and Caird et al[69] have shown that most of the cases (80%) of severe COPD are associated with right axis deviation. We could replicate this in our study population. In our study the distribution of severity of COPD status in relation to ECG changes is meaningfully significant. Increased incidence of ECG changes is seen in moderate COPD compared to mild COPD (elevated percentage difference of 44.3 points, 95% higher) and increased incidence of ECG changes is also seen in severe COPD compared to moderate COPD (elevated percentage difference of 36.6 points, 44% higher). This could be attributed to the higher level of deterioration in lung function and pulmonary hypertension in these individuals.

In our study the distribution of PHT status in relation to ECG changes is meaningfully significant. Increased incidence of ECG changes is seen in moderate PHT compared to mild PHT (elevated percentage difference of 50.00 points, 100% higher) and increased incidence of ECG changes also seen in severe PHT

compared to moderate PHT (elevated percentage difference of 30.8 points, 32% higher).

In our study the distribution of severity of COPD status in relation to ECG changes is meaningfully significant. Increased incidence of ECG changes is seen in moderate COPD compared to mild COPD (elevated percentage difference of 44.3 points, 95% higher) and increased incidence of ECG changes is also seen in severe COPD compared to moderate COPD (elevated percentage difference of 36.6 points, 44% higher).

In our study the distribution of mean number of exacerbations between the severity of COPD categories is meaningfully significant. This is evident by the decreased mean number of exacerbations in mild category compared to moderate category (mean reduction difference of 4.91 episodes, 89% lower) and decreased mean number of exacerbations in moderate category compared to severe category (mean reduction difference of 8.84episodes, 62% lower).

In our study the distribution of mean Hb levels between the severity of COPD categories is meaningfully significant. This is evident by the increased mean Hb levels in mild category compared to moderate category (mean elevated difference of 2.17 mg/dl, 20% higher) and increased mean Hb levels in moderate category compared to severe category (mean elevated difference of 0.19 mg/dl, 2% higher).

Our study shows that there is no significant correlation exists between Body Mass Index (BMI) and the Severity of COPD.

A multiple component staging system combining $FEV_1$, 6-min walking distance, dyspnea scored with the MMRC scale, and $PaO_2$ was reported to better describe health-care resources utilization among COPD patients in different geographic areas when compared to international COPD classifications (ATS, British Thoracic Society, and GOLD)[86]. The BODE index was also reported to be a much better predictor of the severity in COPD acute exacerbations than $FEV_1$[2]. Our findings of the usefulness of the BODE index in predicting hospitalization for COPD are also supported by the findings of a prospective study[29] of risk factors of hospital readmissions for COPD exacerbation. In that study, a strong association between the usual physical activity and reduced risk of COPD readmission was demonstrated. Moreover, the association did not change when adjusted for $FEV_1$ or nutritional status. These results are in agreement with the increased risk of COPD hospital admission associated with a limited 6-min walking test reported by another group of investigators[23]. Therefore, it may be speculated that the superior value of the BODE index compared to $FEV_1$ in predicting hospital admissions for COPD that we have observed, is accounted for by the evaluation of physical performance status among the individual components of the BODE scoring system. Admission to the hospital and heavy use of health-care resources is a common feature of COPD. A clinical implication of the present study is that the

BODE scoring system may prove to be helpful in health-care resource allocation and in guiding therapy for individual patients in the future. This multistage scoring system, which incorporates variables that can be evaluated easily in any office setting, should not be difficult or costly to implement routinely. As the BODE index can provide useful prognostic information of survival and hospitalization, the findings of the present study are in support of the utility of the BODE index as an assessment tool for COPD patients.

# LIMITATIONS OF THE STUDY

- Only a small number of population is taken for the study.
- This is a hospital based study and hence it may not be the representative of the general population.
- The results of this study should be very cautiously used outside India, since there is no systematic comparisons of various regional manifestations of COPD.
- Only males were included in the study and the hence, the results of this study cannot be used in female COPD patients.
- As a prospective cross sectional study, the present analysis has its own limitations, in its ability to elucidate, whether improving this BODE Score would reverse the various parameters analyzed.
- Alternate causes and medication effects influencing the parameters analyzed should also be considered.

# CONCLUSIONS

- BODE Index can be used as a very useful and reliable index to assess the severity of Chronic Obstructive Pulmonary Disease (COPD).
- BODE index is directly correlated with the number of exacerbations.
- As the Smoking intensity and the Smoking Pack Years increases the BODE Index also increases.
- BODE index predicts the frequent hospitalisations due to acute COPD exacerbations.
- Hemoglobin decreases in the severe form of disease.
- Cardiac effects of the disease as studied by the 2D ECHO PHT increases with the severity of COPD as assessed by BODE index.
- BODE index directly correlates with nutritional derangement in patients with COPD as evidenced by the changes in BMI.
- ECG changes is a good, consistent and direct predictor of Mild, Moderate and Severe COPD.

# SUMMARY

Thus our study concludes that BODE Index is a reliable method to predict hospitalization and the severity of cardiac involvement in patients with COPD. Since the assessment of BODE index requires only a spirometer, which is relatively inexpensive and can easily be made available, this index could be of great practical value in a primary health care (PHC) setup to identify individuals who are at need for further evaluation in a higher center. Thus the BODE index can be used for judicious referral of patients with COPD thereby preventing the wastage of the limited resources available in developing country like India.

# SCOPE FOR FUTURE STUDIES

This study has many significant observations with potential implications. This study concludes that BODE Index is a very reliable method to predict hospitalization and the severity of cardiac involvement in patients with COPD. Future studies are needed to assess whether it can be used as a reliable index to monitor the disease progression. Studies are also needed to assess whether reduction in BODE index improves the disease status. Further research should be done in the hemoglobin concentration with the disease progression.

Future research should also aim at finding the intervention measures which have the greatest impact on BODE index and thereby the severity of the disease. We do not know whether it will be a useful indicator of the outcome in clinical trials, the degree of utilization of health care resources, or the clinical response to therapy. More clinical studies are needed in this regard.

To simply summarize, the BODE Index scoring system is a reliable index to predict frequent hospitalizations and the severity of cardiac involvement in patients with COPD. Besides its excellent predictive power with regard to outcome, the BODE index is simple to calculate with the help of spirometer and requires no special equipment. This makes it a practical tool of potentially widespread applicability.

# BIBLIOGRAPHY


1. National Heart, Lung and Blood institute. Morbidity and mortality chart book on cardiovascular, lung and blood diseases. Bethesda, Maryland: Us department of health and human services, public health service, national institute of health accessed at http://www.nhlbi.nih.gov/ resources/docs/cht-book.htm; 2004.

2. Kian Chung Ong, FRCP; Arul Earnest, MSc; and Suat-Jin Lu, MBBS: A multidimensional grading system (BODE INDEX) as a predictor of hospitalization for COPD. Chest 2005; 128:3810-3816

3. Global initiative for chronic obstructive lung disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. 2007; available from www.goldcopd.com: accessed Oct 5, 2008.

4. Emil F. M. Wouters, MD, PhD, FCCP; Eva C. Creutzberg, PhD and Annemie M. W. J. Schols, PhD. Systemic effects in COPD. Chest. 2002 May;121(5 Suppl):127S-130S.

5. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnoea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med 2004;**350**:1005–12

6. Sean D. Sullivan, PhD; Scott D. Ramsey, MD, PhD and Todd A. Lee, Pharm D. The Economic Burden of COPD. Chest. 2000;117:5S-9S

7. Sidney S. Braman, MD, FACP, FCCP. Update on the ATS Guidelines

for COPD. Medscape Pulmonary Medicine. 2005; 9(1) ©2005 Medscape.

8. Murray CJL, Lopez AD, evidence based health policy lessons from the global burden of diseases study. Science 1996; 274: 740-3

9. Murray CJL, Lopez AD, global burden of diseases; a comprehensive assessment of morbidity and mortality from diseases, injuries and risk factors in 1990 and projected to 2020 Cambridge MA; Harvard university press 1996

10. Kim DS, Kim YS, Jung KS, Chang JH, Lim CM, Lee JH, etal. Prevalence of chronic obstructive pulmonary disease in Korea : a population based spirometry survey . Am J Respir care Med 2005;172:842-7

11. Jindal SK, Gupta D, Aggarwal AN. Guidelines for management of chronic obstructive pulmonary disease in India: a guide for physicians (2003). Indian J Chest Dis Allied Sci 2004; 46: 137-93.

12. Stoller JK, Aboussouan LS. Alpha1-antitrypsin deficiency. Lancet 2005;365(9478):2225-36.

13. Blanco I, de Serres FJ, Fernandez-Bustillo E, Lara B, Miravitlles M. Estimated numbers and prevalence of PI*S and PI*Z alleles of alpha1-antitrypsin deficiency in European countries. Eur Respir J 2006;27(1):77-84.

14. Stoller JK, Aboussouan LS. Alpha1-antitrypsin deficiency. Lancet 2005;365(9478):2225-36.

15. Blanco I, de Serres FJ, Fernandez-Bustillo E, Lara B, Miravitlles M. Estimated numbers and prevalence of PI*S and PI*Z alleles of alpha1-antitrypsin deficiency in European countries. Eur Respir J 2006; 27(1):77-84.

16. Jindal SK, Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, et al. A multicentric study on epidemiology of chronic obstructive pulmonary disease and its relationship with tobacco smoking and environmental tobacco smoke exposure. Indian J Chest Dis Allied Sci 2006;48(1):23-9.

17. Al-Fayez SF, Salleh M, Ardawi M, AZahran FM. Effects of sheesha and cigarette smoking on pulmonary function of Saudi males and females. Trop Geogr Med 1988;40(2):115-23.

18. Smith CA, Harrison DJ. Association between polymorphism in gene for microsomal epoxide hydrolase and susceptibility to emphysema. Lancet 1997;350(9078):630-3.

19. The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General, Department of Health and Human Services. Washington, DC, US; 2006.

20. Eisner MD, Balmes J, Katz BP, Trupin L, Yelin E, Blanc P. Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease. Environ Health Perspect 2005;4:7-15.

21. Leuenberger P, Schwartz J, Ackermann-Liebrich U, Blaser K, Bolognini G, Bongard JP, et al. Passive smoking exposure in adults and chronic respiratory symptoms (SAPALDIA Study). Swiss Study on Air Pollution and Lung Diseases in Adults, SAPALDIA Team. Am J Respir Crit Care Med 1994;150(5 Pt 1):1222-8.

22. Dayal HH, Khuder S, Sharrar R, Trieff N. Passive smoking in obstructive respiratory disease in an industrialized urban population. Environ Res 1994;65(2):161-71.

23. Balmes J, Becklake M, Blanc P, Henneberger P, Kreiss K, Mapp C, et al. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. Am J Respir Crit Care Med 2003;167(5):787-97

24. Warwick H, Doig A. Smoke the killer in the kitchen: Indoor air pollution in developing countries. ITDG Publishing, 103-105 Southampton Row, London WC1B HLD, UK 2004: URL: http://www.itdgpublishing.org.uk.

25. Ezzati M. Indoor air pollution and health in developing countries. Lancet 2005;366(9480):104-6.

26. Smith KR, Mehta S, Maeusezahl-Feuz M. Indoor air-pollution from household solid fuel use. In: Ezzati M., Lopez, AD, Rodgers M., Murray CJ, eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva: World Health Organization; 2004.

27. Mishra V, Dai X, Smith KR, Mika L. Maternal exposure to biomass smoke and reduced birth weight in Zimbabwe. Ann Epidemiol 2004;14(10):740-7.

28. Boman C, Forsberg B, Sandstrom T. Shedding new light on wood smoke: a risk factor for respiratory health. Eur Respir J 2006;27(3): 446-7.

29. Oroczo-Levi M, Garcia -Aymerich J, Villar J, Ramirez-Sarmiento A, Anto JM, Gea J. Wood smoke exposure and risk of chronic obstructive pulmonary disease. Eur Respir J 2006;27:542-6.

30. Sezer H, Akkurt I, Guler N, Marakoglu K, Berk S. A case-control study on the effect of exposure to different substances on the development of COPD. Ann Epidemiol 2006;16(1):59-62.

31. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance– United States, 1971-2000. MMWR Surveill Summ 2002;51(6):1-16.

32. Xu X, Weiss ST, Rijcken B, Schouten JP. Smoking, changes in smoking habits, and rate of decline in FEV1: new insight into gender differences. Eur Respir J 1994;7(6):1056-61.

33. Anthonisen NR, Connett JE, Kiley JP, Altose MD, Bailey WC, Buist AS, et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. JAMA 1994;272(19):1497-505.

34. Silverman EK, Weiss ST, Drazen JM, Chapman HA, Carey V, Campbell EJ, et al. Gender-related differences in severe, early-onset chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000;162(6):2152-8.

35. Tager IB, Segal MR, Speizer FE, Weiss ST. The natural history of forced expiratory volumes. Effect of cigarette smoking and respiratory symptoms. Am Rev Respir Dis 1988;138(4):837-49.

36. Barker DJ, Godfrey KM, Fall C, Osmond C, Winter PD, Shaheen SO. Relation of birth weight and childhood respiratory infection to adult lung function and death from chronic obstructive airways disease. BMJ 1991;303(6804):671-5.

37. Shaheen SO, Barker DJ, Shiell AW, Crocker FJ, Wield GA, Holgate ST. The relationship between pneumonia in early childhood and impaired lung function in late adult life. Am J Respir Crit Care Med 1994;149(3 Pt 1):616-9.

38. Prescott E, Lange P, Vestbo J. Socioeconomic status, lung function and admission to hospital for COPD: results from the Copenhagen City Heart Study. Eur Respir J 1999;13(5):1109-14.

39. Tao X, Hong CJ, Yu S, Chen B, Zhu H, Yang M. Priority among air pollution factors for preventing chronic obstructive pulmonary disease in Shanghai. Sci Total Environ 1992;127(1-2):57-67.

40. US Centers for Disease Control and Prevention. Criteria for a recommended standard: occupational exposure to respirable coal mine dust: National Institute of Occupational Safety and Health; 1995.

41. Neergaard Kv, Wirz K. U¨ ber eine Methode zur Messung der Lungenelastizita¨ t am lebenden Menschen, insbesondere beim Emphysem. Z Klin Med 1927;105:35–48.

42. Christie R. The elastic properties of the emphysematous lung and their clinical significance. J Clin Invest 1934;13:295.

43. Corbin RP, Loveland M, Martin RR, Macklem PT. A four-year followup study of lung mechanics in smokers. Am Rev Respir Dis 1979;120: 293– 304.

44. Hogg J, Chu F, Utokaparch S, Woods R, Elliott W, Buzatu L, Cherniack R, Rogers R, Sciurba F, Coxson H, et al. The nature of small-airway obstruction in chronic obstructive pulmonary disease. N Engl J Med 2004;350:2645–2653.

45. Laurell CB, Eriksson S. The electrophoretic alpha-globulin pattern of serum in alpha-antitrypsin deficiency. Scand J Clin Invest 1963;15:132–140.

46. Gross P, Pfitzer E, Tolker E, Babyak M, Kaschak M. Experimental emphysema: its production with papain in normal and silicotic rats.Arch Environ Health 1965;11:50–58.

47. Kuhn C, Yu S, Chraplyvy M, Linder H, Senior RM. The induction of emphysema with elastase: changes in connective tissue. Laboratory Investigation 1976;34:372–380.

48. Senior RM, Tegner H, Kuhn C, Ohlsson K, Starcher BC, Pierce JA. The induction of pulmonary emphysema induced with human leukocyte elastase. Am Rev Respir Dis 1977;116:469.

49. Janoff A, Sloan B, Weinbaum G, Damiano V, Sandhaus RA, Elias J, Kimbel P. Experimental emphysema induced with purified human neutrophil elastase: tissue localization of the instilled protease. Am Rev Respir Dis 1977;115:461.

50. Snider G, Lucey EC, Christensen TG, Stone PJ, Calore JD, Catanese A, Franzblau C. Emphysema and bronchial secretory cell metaplasia induced in hamsters by human neutrophil products. Am Rev Respir Dis 1984;129:155– 160.

51. Kao RC, Wehner NG, Skubitz KM, Gray BH, Hoidal JR. Proteinase 3: A distinct human polymorphonuclear leukocyte proteinase that produces emphysema in hamsters. J Clin Invest 1988;82:1963–1973.

52. Eidelman D, Saetta MP, Ghezzo H, Wang N-S, Hoidal JR, King M, Cosio MG. Cellularity of the alveolar walls in smokers and its relation to lung destruction: functional implications. Am Rev Respir Dis 1990;141:1547– 1552.

53. Finkelstein R, Fraser RS, Ghezzo H, Cosio MG. Alveolar inflammation and its relation to emphysema in smokers. Am J Respir Crit Care Med 1995;152:1666–1672.

54. Senior RM, Griffin GL, Fliszar CJ, Shapiro SD, Goldberg GI, Welgus HG. Human 92- and 72-kilodalton type IV collagenases are elastases. J Biol Chem 1991;266:7870–7875.

55. Shapiro SD, Kobayashi DK, Ley TJ. Cloning and characterization of a unique elastolytic metalloproteinase produced by human alveolar macrophages. J Biol Chem 1993;268:23824–23829.

56. Chapman HAJ, Stone OL, Vavrin Z. Degradation of fibrin and elastin by intact human alveolar macrophages in vitro. Characterization of a plasminogen acivator and its role in matrix degradation. J Clin Invest 1984;73:806–815.

57. Campbell E, Senior R, Welgus H. Extracellular matrix injury during lung inflammation. Chest 1987;92:161–167.

58. Retamales I, Elliott W, Meshi B, Coxson H, Pare P, Sciurba F, Rogers R, Hayashi S, Hogg J. Amplification of inflammation in emphysema and its association with latent adenoviral infection. Am J Respir Crit Care Med 2001;164:469–473.

59. Senior RM, Griffin GL, Mecham RP. Chemotactic activity of elastinderived peptides. J Clin Invest 1980;66:859–862.

60. Huninghake GW, Davidson JM, Rennard S, Szapiel S, Gadek JE, Crystal RG. Elastin fragments attract macrophage precursors to diseased sites in pulmonary emphysema. Science 1981;212:925–927.

61. Grumelli S, Corry D, Song L, Green L, Huh J, Hacken J, Espada R, Bag R, Lewis D, Kheradmand F. An immune basis for lung parenchymal destruction in chronic obstructive pulmonary disease and emphysema. PLoS Med. 2004;1:e8.

62. Churg A, Wang R, Tai H, Wang X, Xie C, Dai J, Shapiro S, Wright J. Macrophage metalloelastase mediates acute cigarette smoke-induced inflammation via tumor necrosis factor-alpha release. Am J Respir Crit Care Med 2003;167:1083–1089.

63. Ito K, Ito M, Elliott M, Cosio MG, Caramori G, Kon O, Barczyk A, Hayashi S, Adcock I, Hogg J, et al. Decreased histone deacetylase activity in chronic obstructive pulmonary disease: Relationship to severity. N Engl J Med.

64. Kasahara Y, Tuder RM, Cool CD, Lynch DA, Flores SC, Voelkel NF. Inhibition of VEGF receptors causes lung cell apoptosis and emphysema. J Clin Invest 2000;106:1311–1319.

65. Aoshiba K, Yokohori N, Nagai A. Alveolar wall apoptosis causes lung destruction and emphysematous changes. Am J Respir Cell Mol Biol 2003;28:552–562.

66. Rahman, I, Morrison, D, Donaldson, K, et al (1996) Systemic oxidative stress in asthma, COPD, and smokers. Am J Respir Crit Care Med 154,1055-1060

67. Schols, AM, Buurman, WA, Staal van den Brekel, AJ, et al (1996) Evidence for a relation between metabolic derangements and increased levels of inflammatory mediators in a subgroup of patients with chronic obstructive pulmonary disease. Thorax 51,819-824

68. Takabatake, N, Nakamura, H, Abe, S, et al (1999) Circulating leptin in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 159,1215-1219

69. Engelen, MP, Schols, AM, Baken, WC, et al (1994) Nutritional depletion in relation to respiratory and peripheral skeletal muscle function in out-patients with COPD. Eur Respir J 7,1793-1797

70. Schols, AM, Soeters, PB, Dingemans, AM, et al (1993) Prevalence and characteristics of nutritional depletion in patients with stable COPD eligible for pulmonary rehabilitation. Am Rev Respir Dis 147,1151-1156

71. Baarends, EM, Schols, AM, Mostert, R, et al (1997) Peak exercise response in relation to tissue depletion in patients with chronic obstructive pulmonary disease. Eur Respir J 10,2807-2813

72. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 2001;163:1256-1276.

73. Definitions, epidemiology, pathophysiology, diagnosis, and staging. Am J Respir Crit Care Med 1995;152:Suppl: S78-S83.

74. Siafakas NM, Vermeire P, Pride NB, et al. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). Eur Respir J 1995;8:1398-1420.

75. Anthonisen NR, Wright EC, Hodgkin JE. Prognosis in chronic obstructive pulmonary disease. Am Rev Respir Dis 1986;133:14-20.

76. Burrows B. Predictors of loss of lung function and mortality in obstructive lung diseases. Eur Respir Rev 1991;1:340-5.

77. Domingo-Salvany A, Lamarca R, Ferrer M, et al. Health-related quality of life and mortality in male patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2002;166:680-685.

78. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest 2002;121:1434-1440.

79. Pulmonary rehabilitation - 1999. Am J Respir Crit Care Med 1999;159:1666-1682.

80. Li, Benoit-Connors ML, Reardon JZ, ZuWallack RL. Variables related to increased mortality following out-patient pulmonary rehabilitation. Eur Respir J 1996;9:431-435.

81. Schols AM, Slangen J, Volovics L, Wouters EF. Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1998;157:1791-1797.

82. Landbo C, Prescott E, Lange P, Vestbo J, Almdal TP. Prognostic value of nutritional status in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1999;160:1856-1861.

83. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-117.

84. Miyamoto S, Nagaya N, Satoh T, et al. Clinical correlates and prognostic significance of six-minute walk test in patients with primary pulmonary hypertension: comparison with cardiopulmonary exercise testing. Am J Respir Crit Care Med 2000;161:487-492.

## ANNEXURES

## PROFORMA

Name : Age/sex :

Address : IP / OP No:

Contact No :

Occupatipon :

Diagnosis :

Height :

Weight :

BMI :

**Chief Complaints:**

**History:**

- H/O Cough with Expectoration
- H/O Fever
- H/O LOW
- H/O LOA
- H/O Breathing difficulty
- H/O Easy Fatigability
- H/O Chest pain
- H/O Palpitations
- H/O Swelling of both legs

**Past History:**

- H/O DM / CAD/ Renal disease/ Liver disease/ Old PTB/ CVA/ any Malignancy
- H/O any previous Drug intake

**Personal History:**

- H/O Smoking and Smoking Index is calculated
- H/O Alcoholic

**Examination:**

- **General Examination:** Built & Nourishment, Pallor, Icteric, Cyanosis, Clubbing, Lymphadenopathy, Pedal edema.
- **Systemic Examination:** CVS, Abdomen, CNS.
- **Examination of Respiratory system:** Inspection, Palpation, Percussion, Auscultaion.

**Investigations:**

- Complete Hemogram
- ECG
- ECHOCARDIOGRAM
- Spirometry
- CXR PA view

**QUESTIONNAIRE:**

H/O Smoking : Yes / No, If Yes, How many years ___

: No of Packs/day

Smoking Index :

H/O Breathlessness : Yes / No, If Yes, Grade _____

H/O Cough with expectoration: Yes / No, If yes, how frequently in last

2 years____

H/O Previous Hospitalisation: Yes / No, If Yes, How many times?

# MASTER CHART

| PRELIMINARY INF | | HISTORY | | | GENERAL EXAMINATION | | | INVESTIGATIONS | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SL NO | AGE | SMOKER | Smoking in Pack Years | No of Exacerbations | Height(cm) | Weight(Kg) | BMI | Hb(gms%) | ECG | | ECHO | 6 min Walk test | FEV1 (%) | FEV1/FVC (%) | Post Bronchodilator | MMRC grade | BODE score | Severity of COPD |
| | | | | | | | | | P' Pu | RAD | PHT | | | | | | | |
| 1 | 50 | Y | 18 | 12 | 158 | 51 | 20.4 | 10.1 | Y | Y | Severe | 145 | 32 | 71 | 36 | 3 | 9 | Severe |
| 2 | 57 | Y | 9 | 4 | 156 | 37 | 15.2 | 10.8 | N | N | Mild | 445 | 91 | 70 | 94 | 1 | 1 | Mild |
| 3 | 50 | Y | 1 | 5 | 183 | 62 | 18.5 | 11.3 | N | N | Mild | 600 | 94 | 98 | 100 | 0 | 0 | Mild |
| 4 | 60 | Y | 8 | 1 | 140 | 47 | 22.3 | 9.5 | Y | Y | Moderate | 370 | 67 | 127 | 70 | 1 | 0 | Mild |
| 5 | 50 | Y | 6 | 2 | 155 | 59 | 24.5 | 9.9 | N | N | Mild | 450 | 113 | 106 | 117 | 1 | 0 | Mild |
| 6 | 47 | Y | 4 | 3 | 164 | 67 | 24.9 | 10.1 | N | N | Moderate | 475 | 80 | 90 | 84 | 1 | 0 | Mild |
| 7 | 51 | Y | 20 | 14 | 164 | 63 | 23.4 | 9.2 | Y | Y | Severe | 135 | 25 | 60 | 29 | 3 | 8 | Severe |
| 8 | 60 | Y | 7 | 1 | 165 | 48 | 17.6 | 10.3 | N | N | Mild | 480 | 95 | 91 | 99 | 1 | 1 | Mild |
| 9 | 54 | Y | 8 | 5 | 167 | 56 | 20.07 | 11.1 | Y | Y | Moderate | 320 | 48 | 87 | 51 | 2 | 5 | Moderate |
| 10 | 65 | Y | 6 | 5 | 157 | 45 | 18.2 | 7.5 | Y | Y | Moderate | 320 | 48 | 112 | 51 | 2 | 5 | Moderate |
| 11 | 70 | Y | 9 | 5 | 160 | 43 | 16.7 | 8.2 | N | N | Moderate | 340 | 61 | 127 | 64 | 1 | 3 | Moderate |
| 12 | 65 | Y | 20 | 16 | 157 | 53 | 21.5 | 9.9 | Y | Y | Moderate | 175 | 40 | 101 | 44 | 3 | 6 | Severe |
| 13 | 65 | Y | 22 | 13 | 164 | 61 | 22.68 | 7.8 | Y | Y | Severe | 160 | 46 | 87 | 73 | 3 | 6 | Severe |
| 14 | 58 | Y | 7 | 0 | 159 | 59 | 23.33 | 9 | N | N | No | 400 | 81 | 85 | 88 | 1 | 0 | Mild |
| 15 | 50 | Y | 6 | 0 | 166 | 81 | 29.39 | 12.5 | N | N | No | 495 | 98 | 106 | 104 | 1 | 0 | Mild |
| 16 | 60 | Y | 22 | 15 | 167 | 46 | 16.49 | 8.1 | Y | Y | Severe | 120 | 34 | 116 | 34 | 3 | 9 | Severe |
| 17 | 55 | Y | 24 | 14 | 168 | 50 | 17.71 | 7.1 | Y | Y | Severe | 110 | 24 | 56 | 32 | 4 | 10 | Severe |
| 18 | 62 | Y | 9 | 10 | 175 | 80 | 26.12 | 8 | N | N | Severe | 132 | 32 | 37 | 36 | 3 | 8 | Severe |
| 19 | 69 | Y | 7 | 4 | 156 | 73 | 30 | 9.4 | Y | Y | Moderate | 175 | 42 | 100 | 66 | 2 | 5 | Moderate |
| 20 | 50 | Y | 6 | 1 | 176 | 96 | 30.99 | 11.2 | N | N | No | 458 | 101 | 121 | 104 | 1 | 0 | Mild |
| 21 | 72 | Y | 7 | 5 | 154 | 76 | 32.04 | 8.6 | Y | Y | Severe | 230 | 44 | 134 | 53 | 2 | 5 | Moderate |
| 22 | 42 | Y | 8 | 0 | 172 | 63 | 21.29 | 9.2 | N | N | Mild | 447 | 106 | 99 | 108 | 1 | 0 | Mild |
| 23 | 52 | Y | 9 | 0 | 158 | 66 | 26.43 | 13 | N | N | No | 500 | 92 | 108 | 96 | 1 | 0 | Mild |
| 24 | 50 | Y | 5 | 0 | 168 | 75 | 22.39 | 11.5 | N | N | Mild | 320 | 62 | 80 | 66 | 1 | 2 | Mild |
| 25 | 50 | Y | 4 | 1 | 159 | 68 | 26.98 | 12.3 | N | N | Mild | 252 | 65 | 108 | 68 | 1 | 2 | Mild |
| 26 | 62 | Y | 18 | 14 | 162 | 65 | 24.76 | 9.1 | Y | Y | Severe | 150 | 27 | 46 | 31 | 3 | 7 | Severe |
| 27 | 70 | Y | 6 | 0 | 163 | 40 | 15.05 | 9.9 | N | N | Mild | 350 | 77 | 106 | 79 | 1 | 1 | Mild |
| 28 | 59 | Y | 20 | 16 | 152 | 48 | 20.77 | 11.8 | N | N | Mild | 162 | 49 | 56 | 53 | 3 | 7 | Severe |
| 29 | 52 | Y | 30 | 17 | 159 | 52 | 20.56 | 6.5 | Y | Y | Severe | 220 | 36 | 60 | 40 | 3 | 7 | Severe |
| 30 | 60 | Y | 9 | 7 | 162 | 58 | 22.1 | 8.9 | Y | Y | Moderate | 300 | 56 | 88 | 60 | 2 | 3 | Moderate |
| 31 | 68 | Y | 8 | 6 | 167 | 62 | 22.23 | 9.3 | N | N | Moderate | 275 | 60 | 103 | 64 | 2 | 3 | Moderate |
| 32 | 70 | Y | 4 | 0 | 158 | 50 | 20.02 | 8.5 | N | N | Mild | 400 | 67 | 108 | 71 | 1 | 1 | Mild |
| 33 | 54 | Y | 2 | 0 | 157 | 50 | 20.28 | 9 | N | N | No | 420 | 70 | 101 | 74 | 0 | 1 | Mild |
| 34 | 56 | Y | 7 | 0 | 160 | 58 | 22.65 | 11 | N | N | No | 470 | 72 | 102 | 76 | 1 | 0 | Mild |
| 35 | 49 | Y | 6 | 0 | 162 | 58 | 22.1 | 10 | N | N | Mild | 375 | 65 | 108 | 70 | 1 | 0 | Mild |
| 36 | 58 | Y | 8 | 5 | 159 | 54 | 21.3 | 8.8 | Y | Y | Severe | 300 | 61 | 107 | 65 | 2 | 4 | Moderate |
| 37 | 62 | Y | 9 | 5 | 154 | 49 | 20.66 | 7.5 | N | N | Moderate | 320 | 54 | 90 | 59 | 1 | 3 | Moderate |
| 38 | 67 | Y | 6 | 0 | 167 | 60 | 21.5 | 9.4 | N | N | Mild | 450 | 67 | 108 | 71 | 0 | 0 | Mild |
| 39 | 70 | Y | 4 | 0 | 168 | 62 | 21.9 | 11.6 | N | N | No | 475 | 70 | 102 | 74 | 1 | 0 | Mild |
| 40 | 72 | Y | 7 | 5 | 159 | 52 | 20.5 | 8.3 | Y | Y | Moderate | 200 | 50 | 104 | 54 | 2 | 5 | Moderate |
| 41 | 63 | Y | 6 | 1 | 160 | 57 | 22.26 | 9.4 | N | N | Mild | 320 | 62 | 103 | 66 | 1 | 2 | Mild |
| 42 | 53 | Y | 22 | 17 | 162 | 58 | 22.1 | 10.2 | Y | Y | Severe | 110 | 27 | 75 | 31 | 4 | 9 | Severe |
| 43 | 50 | Y | 8 | 4 | 164 | 60 | 22.3 | 7.6 | N | N | Severe | 175 | 49 | 82 | 53 | 2 | 5 | Moderate |
| 44 | 62 | Y | 6 | 0 | 157 | 52 | 21.09 | 13.2 | N | N | Mild | 400 | 67 | 116 | 71 | 1 | 1 | Mild |
| 45 | 50 | Y | 9 | 4 | 183 | 62 | 18.5 | 7.9 | N | N | Moderate | 227 | 58 | 67 | 61 | 2 | 4 | Moderate |
| 46 | 60 | Y | 7 | 0 | 165 | 48 | 17.6 | 14 | N | N | Mild | 480 | 95 | 91 | 99 | 1 | 1 | Mild |
| 47 | 65 | Y | 24 | 14 | 157 | 53 | 21.5 | 9.2 | N | N | Severe | 175 | 40 | 101 | 71 | 3 | 6 | Severe |
| 48 | 57 | Y | 5 | 0 | 156 | 37 | 15.2 | 12.3 | N | N | Mild | 445 | 91 | 70 | 94 | 1 | 1 | Mild |
| 49 | 50 | Y | 20 | 16 | 158 | 51 | 20.4 | 9.2 | Y | Y | Severe | 145 | 32 | 71 | 36 | 3 | 9 | Severe |
| 50 | 72 | Y | 9 | 6 | 154 | 76 | 32.04 | 8.3 | N | N | Severe | 230 | 44 | 134 | 53 | 2 | 5 | Moderate |
| 51 | 67 | Y | 6 | 0 | 161 | 60 | 23.14 | 12.6 | N | N | No | 440 | 81 | 100 | 82 | 1 | 0 | Mild |
| 52 | 54 | Y | 22 | 14 | 166 | 62 | 22.4 | 7.5 | Y | Y | Severe | 120 | 35 | 82 | 70 | 3 | 8 | Severe |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 53 | 50 | Y | 5 | 0 | 166 | 55 | 19.95 | 9.2 | N | N | Mild | 375 | 75 | 94 | 78 | 1 | 1 | Mild |
| 54 | 50 | Y | 8 | 0 | 162 | 46 | 17.5 | 11.2 | N | N | Mild | 480 | 127 | 124 | 130 | 1 | 1 | Mild |
| 55 | 50 | Y | 6 | 0 | 159 | 65 | 25.7 | 13 | N | N | No | 500 | 112 | 123 | 114 | 0 | 0 | Mild |
| 56 | 55 | Y | 24 | 16 | 165 | 50 | 18.3 | 6.9 | Y | Y | Severe | 138 | 26 | 108 | 44 | 3 | 9 | Severe |
| 57 | 68 | Y | 22 | 17 | 161 | 65 | 25.07 | 7.5 | Y | Y | Severe | 128 | 20 | 86 | 35 | 3 | 8 | Severe |
| 58 | 50 | Y | 20 | 12 | 178 | 50 | 15.7 | 8.8 | Y | Y | Severe | 100 | 14 | 60 | 18 | 4 | 10 | Severe |
| 59 | 52 | Y | 7 | 0 | 154 | 50 | 21.08 | 9.1 | N | N | Mild | 452 | 138 | 114 | 140 | 0 | 1 | Mild |
| 60 | 62 | Y | 6 | 0 | 175 | 66 | 21.55 | 12.5 | N | N | No | 475 | 119 | 114 | 121 | 0 | 0 | Mild |
| 61 | 49 | Y | 22 | 14 | 163 | 48 | 18.06 | 8.9 | Y | Y | Severe | 184 | 42 | 92 | 51 | 3 | 7 | Severe |
| 62 | 68 | Y | 5 | 1 | 166 | 78 | 28.3 | 10.5 | N | N | Mild | 448 | 96 | 103 | 92 | 0 | 0 | Mild |
| 63 | 53 | Y | 9 | 2 | 173 | 55 | 18.37 | 10.9 | N | N | Mild | 375 | 69 | 89 | 70 | 1 | 1 | Mild |
| 64 | 55 | Y | 20 | 15 | 175 | 48 | 15.67 | 7.9 | Y | Y | Severe | 138 | 31 | 81 | 35 | 2 | 8 | Severe |
| 65 | 73 | Y | 6 | 2 | 156 | 38 | 15.6 | 12.4 | N | N | Mild | 490 | 114 | 138 | 118 | 0 | 1 | Mild |
| 66 | 45 | Y | 24 | 10 | 172 | 68 | 22.98 | 6.8 | Y | Y | Severe | 110 | 20 | 77 | 24 | 4 | 9 | Severe |
| 67 | 50 | Y | 7 | 1 | 174 | 60 | 19.8 | 9.3 | N | N | Mild | 500 | 101 | 109 | 104 | 1 | 1 | Mild |
| 68 | 67 | Y | 8 | 1 | 170 | 61 | 21.1 | 10.9 | N | N | No | 398 | 93 | 124 | 99 | 1 | 0 | Mild |
| 69 | 62 | Y | 20 | 14 | 164 | 49 | 18.2 | 7.8 | Y | Y | Severe | 128 | 31 | 81 | 35 | 3 | 9 | Severe |
| 70 | 70 | Y | 26 | 16 | 154 | 44 | 18.5 | 8.4 | N | N | Severe | 225 | 40 | 87 | 47 | 2 | 6 | Severe |
| 71 | 64 | Y | 6 | 0 | 152 | 56 | 24.2 | 11.4 | N | N | Mild | 375 | 80 | 129 | 84 | 0 | 0 | Mild |
| 72 | 61 | Y | 9 | 0 | 159 | 46 | 18.19 | 12.4 | N | N | Mild | 498 | 113 | 133 | 117 | 1 | 1 | Mild |
| 73 | 65 | Y | 10 | 5 | 160 | 78 | 30.4 | 10.7 | N | N | Moderate | 320 | 52 | 108 | 67 | 2 | 3 | Moderate |
| 74 | 57 | Y | 8 | 0 | 150 | 43 | 19.17 | 12 | N | N | Mild | 500 | 126 | 132 | 130 | 1 | 1 | Mild |
| 75 | 65 | Y | 7 | 12 | 164 | 58 | 21.5 | 9 | N | N | Moderate | 298 | 58 | 77 | 60 | 3 | 4 | Moderate |
| 76 | 57 | Y | 26 | 14 | 172 | 66 | 22.3 | 7.8 | Y | Y | Severe | 120 | 24 | 63 | 30 | 3 | 8 | Severe |
| 77 | 80 | Y | 7 | 0 | 162 | 59 | 22.4 | 7.7 | N | N | Mild | 390 | 66 | 94 | 70 | 1 | 0 | Mild |
| 78 | 56 | Y | 4 | 0 | 158 | 46 | 18.4 | 11.7 | N | N | Mild | 490 | 124 | 116 | 127 | 0 | 1 | Mild |
| 79 | 50 | Y | 4 | 0 | 161 | 56 | 21.6 | 12.1 | N | N | Mild | 350 | 92 | 100 | 92 | 1 | 0 | Mild |
| 80 | 67 | Y | 20 | 15 | 173 | 59 | 19.7 | 10.8 | Y | Y | Severe | 110 | 33 | 71 | 54 | 3 | 9 | Severe |
| 81 | 52 | Y | 6 | 0 | 163 | 45 | 16.9 | 10.3 | N | N | Mild | 375 | 82 | 99 | 92 | 0 | 1 | Mild |

**சுயஒப்புதல் படிவம்**

**ஆய்வு செய்யப்படும் தலைப்பு:**

**இடம்:** பொது மருத்துவத்துவ துரை
அரசு கீழ்பாக்கம் மருத்துவ கல்லூரி மருத்துவமனை
சென்னை

**பங்குபெறுபவரின் பெயர் :**

**பங்குபெறுபவரின் வயது :** **பங்குபெறுபவரின் எண் :**

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக்கொள்ளல்லாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில்பங்கு பெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்க மாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் ஆய்வாளரின் கையொப்பம்

இடம் :

தேதி :

## PATIENT CONSENT FORM

Study detail**: "Evaluation of BODE Index as a predictor of severity and Pulmonary Hypertension in COPD patients, a cross-sectional study at a Tertiary Care Hospital in Chennai"**

Study centre : KILPAUK MEDICAL COLLEGE, CHENNAI
Patients Name :
Patients Age :
Identification Number :

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression:

Patients Name and Address: place date

Signature of investigator :

Study investigator's Name : place date

85. Karoli NA, Rebrov AP. The BODE index as a predictor of unfavourable prognosis in chronic obstructive pulmonary disease. Ter Arkh. 2007;79(3):11-4.

86. Marin, JM, Alonso, J, Sanchez, A, et al Value of current COPD classification versus a multiple component staging system (SCORE) as predictor of health care resource utilization [abstract]. Am J Respir Crit Care Med 2002;165,A43

87. Arcasoy SM, Christie DJ, et al; Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease; Am J RespiR Crit Care Med 167;735, 2003

88. Stevens D, Sharma K, Rich S; severe pulmonary hypertension associated with COPD; Am J Respir Crit Care Med;159:A155;1999

89. Sin DD, Man SF; why are patients with COPD at increased risk of cardiovascular diseases? The potential role of systemic inflammation on COPD; circulation2003;107:1514-9

90. Cirillo DJ, Agarwal Y, Cassano PA; lipids and pulmonary function in third national health and nutrition examination survey; Am J Epidemiol; 2002:155: 842-848